

BUREAU OF HYGIENE AND TROPICAL DISEASES

TROPICAL DISEASES BULLETIN

Vol. 54]

1957

[No. 10

SUMMARY OF RECENT ABSTRACTS *

VIII. TYPHUS GROUP OF FEVERS †

General

WOODWARD (p. 1325) discusses the nature of the processes involved in certain infective diseases, particularly the rickettsial fevers and their action on the capillary endothelium. The rickettsiae may compete with their host cells for certain Krebs-cycle intermediates such as alpha ketoglutamic, succinic, fumaric and other acids, to such an extent that capillary damage may result from diminished production of high-energy phosphate bonds. Various micro-organisms can reside in tissues without causing overt disease—for instance after typhus before the recrudescence known as Brill's disease, and recrudescence may be provoked by stress. He thinks that in future treatment may consist of administration of antibiotics for control of micro-organisms, and the administration of an essential metabolic substance or substrate necessary for proper cell function. HOPPS *et al.* (p. 1329) investigated transamination, oxidative phosphorylation and glutamate incorporation by purified suspensions of *R. mooseri*. Details should be sought in the original.

Intravenous injection of the toxins of *R. prowazeki* and *R. mooseri* into rats and mice causes direct injury to the endothelial cells, with loss of plasma and rise in specific gravity of the blood and haematocrit value (NEVA and SNYDER, p. 170). The (negative) effect of the toxin of murine typhus on certain enzymes was investigated by WATTENBERG (p. 42).

SNYDER (p. 1326) discusses the biology of the rickettsiae, pointing out that infectivity and toxicity can be reduced by freezing and thawing, to be restored by incubation with diphosphopyridine nucleotide (DPN).

* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1956, v. 53. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

† For previous articles on typhus group of fevers in this series, see the October issues of the *Tropical Diseases Bulletin* each year since 1939.

Virulence can be removed by incubation with PABA, but this can be prevented by the addition of DPN and coenzyme A. He discusses the persistence of rickettsiae in man after typhus, which may give rise to Brill's disease, and quotes work which indicates a similar situation in scrub typhus and Rocky Mountain spotted fever.

GIROUD *et al.* (p. 168) examined sera in the Upper Volta region for reactions to various rickettsiae; they found evidence of louse-borne and murine typhus, boutonneuse fever (particularly) and Q fever, and also some reactions to neo-rickettsial antigens. Similarly GIROUD and ROGER (p. 735) found serological evidence of boutonneuse fever, epidemic typhus, Q fever and neo-rickettsial diseases in sera from patients with chorio-retinitis from France, Algeria and the Far East.

LE GAC *et al.* (p. 169) describe varicelliform eruptions in patients from Oubangui with different serological reactions to neo-rickettsial or rickettsial antigens. There seem to be numerous different diseases in which varicella is simulated, other than rickettsialpox.

KHANNA and SINGH (p. 981) found a small proportion of positive results to tests with *Proteus* OXK, OX2 and OX19 (at titres of 1 in 125) in normal persons and non-typhus patients in Amritsar, India.

Proteus OX19 Type. Vectors: Louse and Flea

STEEL and LAWY (p. 1327) report a case of Brill's disease in England. The patient was a Polish woman immigrant who had been in contact with typhus in 1914-18. In Poland 768 sporadic cases of typhus were reported in 1952-54, and of these 39.6% were second infections; the source of the second infection could not usually be traced, but most of these cases occurred in summer. KOSTRZEWSKI (p. 1414) points out that most of the patients with second infections were over 40 years old (unlike those with first infections) and most lived in towns. The time interval between first and second infections showed 2 peaks, at 8-14 years and 30-40 years, which corresponded with the Second and First World War respectively. In 1,077 sera taken in Poland for the Widal test SIENNICKI and RADZISZEWSKA (p. 168) found 31 positive to the typhus complement-fixation reaction, though 9 of these were negative to the Weil-Felix test. Most of these positive sera were thought to be from persons suffering from relapses of typhus; the primary attack of which may have occurred many years (up to 40) earlier.

Brill's disease has now been reported from South America (MEIRA *et al.*, p. 301). In a part of Peru where louse infestation is high MONTOTOYA *et al.* (p. 563) examined over 7,000 sera by the complement-fixation test at low titre, finding evidence of past typhus infection in 94% of the population over the age of 40 in rural areas. They think that recrudescent typhus of the Brill type must be very common, and must form a constant source of fresh infection. In comment, however, Megaw points out that evidence is lacking that lice do actually transmit infection to contacts of

patients with Brill's disease. The authors propose a combination of vaccination and louse control with DDT.

KRYŃSKI and BECLA (p. 429) show that *R. prowazeki* may remain viable much longer at 4°C. when suspended in a mixture of milk and water (35 days) than in phosphate buffer solution (5 days).

In Ethiopia REISS-GUTFREUND (p. 736) isolated rickettsiae—which had the same pathogenic and antigenic properties as the classical strains of *R. prowazeki*—from a goat, 2 sheep and from the ticks *Hyalomma rufipes* and *Amblyomma variegatum*, all infected in nature.

ZARRILLI (p. 41) describes the histopathology of the intestinal walls and mesentery in louse-borne typhus. The underlying lesion is a degenerative vasculitis similar to that found in the vessels of other organs.

VOICULESCU and CARUNTU (p. 301) found the Weil-Felix test positive in 66%, and the complement-fixation test positive in 91%, of a series of patients with typhus in Bucharest.

MILOVANOVIĆ and STOJKOVIĆ (p. 982) used the polysaccharide extracted from *Proteus OX19* as the antigen in the complement-fixation test; it is specific but the test requires an experienced team. The haemolytic test is also specific. 5 different tests were done on normal persons and on a typhus patient (in whom they all showed rising titres); the standard Weil-Felix test usually gives a high titre after the end of the first week. These authors (p. 983) found that by the haemagglutination-inhibition test they could detect the polysaccharide antigen of *Proteus OX19* in a dilution of 1 in 32,000,000 in saline or urine, and they think that this test may be valuable in the early detection of the antigen in the urine of patients with typhus.

In a review of the vaccines which have been used for the prevention of typhus FOX (p. 1328) concludes that the only safe vaccines hitherto have been the killed vaccines, but that a strain (E) of *R. prowazeki* was found in 1943 in Spain which, after 10 yolk-sac passages, suddenly became non-virulent and has remained so. This has been used for vaccination of large numbers of people without serious ill-effect, and the immunity produced appears to be satisfactory, though definite proof that it will prevent the natural disease has not been obtained.

In experiments on the chemoprophylaxis of experimental *R. prowazeki* infection BOGACZ (p. 869) found that 2 compounds (nitrophenyltrichloroethane and aminophenylethane) were more active than pyrimethamine, methoxyphenylpropane, mepacrine and alum.

COBURN (p. 736) states that it is not possible to assess the importance of DDT in the gradual decline of typhus in South Africa; the rhythm of outbreaks seems to be irregular, within periods of 2 years.

Proteus OXK Type. Vector: Mite

SASA (p. 565) gives a full account of tsutsugamushi disease in Japan, distinguishing 3 epidemiological types—a summer type transmitted by

Trombicula akamushi or (possibly) *T. tosa*; an autumn-winter type possibly transmitted by *T. scutellaris*; and an autumn-spring type possibly transmitted by *T. pallida*. He mentions 2 other types, possibly transmitted by *T. palpalis* and *T. intermedia*. SUZUKI (p. 170) gives an account of the bionomics of *Trombicula scutellaris* and its control by application of BHC dust to vegetation.

Experiments on the isolation of *R. tsutsugamushi* from the blood of patients inoculated experimentally showed that the organism could be isolated 2-3 days before the onset of fever and 2-4 days after defervescence following treatment with antibiotics; TAMANO (p. 566) also shows that it could be isolated up to a week after reinoculation of patients who had recovered from previous attacks, even when no fever occurred.

BOZEMAN *et al.* (p. 1415) found that roller-tube cultures of mouse lymphosarcoma cells supported the growth of egg-adapted rickettsiae—including *R. tsutsugamushi*—and have used this technique to study the effect of chloramphenicol on the rickettsiae. It may be possible to study rickettsial synthesis by inhibitor analysis techniques in this culture system.

HAYASHI (p. 305) has found that intracerebral inoculation of mice is the most satisfactory method of serial transmission of *R. tsutsugamushi*.

The pathogenic properties of 4 strains of *R. tsutsugamushi* from Vietnam have been studied by LÊ GAC *et al.* (p. 1415).

KAWAMURA *et al.* (p. 567) report studies on a strain which has been named *R. tamiyai* and which differs in some respects from *R. tsutsugamushi*; it does not produce an eschar, it agglutinates *Proteus OX2* at the same titre as *OXK*, and there is no full cross immunity with *R. tsutsugamushi*. Nevertheless, the disease produced by it closely resembles *tsutsugamushi* disease.

NOSE and TAZAWA (p. 304) investigated the opsonic index in patients infected experimentally with *tsutsugamushi* disease. The index increased in the late incubation period but fell with persisting fever; it was raised by medication, returning to the original level as medication continued.

A dramatic change in the case-mortality rate of *tsutsugamushi* disease took place in Japan when the broad-spectrum antibiotics were introduced. HARA and ABE (p. 1109) report death rates of 20.2% to 45.8% from 1917 to 1948, whereas in 1952-54 there were no deaths in the 273 cases reported. TACHIBANA (p. 302) found that the administration of antibiotics early in scrub typhus tended to prevent the formation of immune body (as judged by the *Proteus OXK* reaction); when they were administered rather later the tests were more often positive and the titres higher.

KATSURA (p. 302) reports an extensive study of the chemotherapy of natural or therapeutically induced *tsutsugamushi* disease, in which he found that aureomycin was the best of several antibiotics tried. A total dosage of 2.5-3.5 gm. of aureomycin or oxytetracycline, starting within the first 3 days and spread over 5-10 days in gradually diminishing daily amounts, was enough gradually to control the fever, without relapse.

With chloramphenicol, erythromycin and magnamycin total doses of 5 gm. or more were needed. In comment Megaw draws attention to the different conditions found in field work, where the patients may come late for treatment and the saving of life is the important point. Antibiotics in this disease do not act as *therapia magna sterilisans*, but protect the body from the risk of death or damage while nature brings about cure and immunity against further attack.

Indeterminate Type. Vector: Tick

JUAREZ (p. 568) describes cases of boutonneuse fever in Spain, in many parts of which it is more common than is generally known. DEPOUX and MERVEILLE (p. 737) report serological evidence, based on complement-fixation tests with various rickettsial antigens, that the *fièvre rouge congolaise* is allied to boutonneuse fever.

McCROAN *et al.* (p. 569) show that Rocky Mountain spotted fever some years ago was more common in the south-eastern United States than was thought, but that the incidence of flea-borne typhus is being reduced. They note that ticks can be controlled on roadsides and paths by insecticides like DDT.

Q fever

GIROUD *et al.* (p. 986) compared the slide-microagglutination test for Q fever with the complement-fixation test; the former was more sensitive than the latter. The same antigen, a suspension in saline of *R. burneti* from the vitelline membrane of a yolk-sac culture, was used for both.

STOKER *et al.* (p. 574) discuss problems raised in the diagnosis of Q fever by complement-fixation tests, pointing out that the 2 commonly used antigens may give different results, and that for clinical diagnosis a rising titre is the important feature. The rickettsia agglutination test did not necessarily show differences between the 2 antigens.

MAZZITELLI (p. 1112) shows that the agglutination test for Q fever may be positive in sheep and cattle when the complement-fixation test is negative.

A soluble immunizing antigen has been prepared from *R. burneti* by COLTER *et al.* (p. 1331), who describe the technique employed.

Q fever is known to occur in 51 countries, and KAPLAN and BERTAGNA (p. 570) recommend 3 tests for use in surveys: (1) complement-fixation tests of workers in abattoirs and fat-rendering plants, (2) inoculation of guineapigs with pooled milk, and post-inoculation complement-fixation tests on the guineapigs, and (3) random complement-fixation tests of individual animals.

In an account of the spread of Q fever from animals to man STOKER and MARMION (p. 573) state that the proved natural hosts are man, 22 species of ticks, the body louse, 8 different mammals, and a pigeon. They discuss some of the questionable features of the infection, such as the extent to which *R. burneti* is transmitted from tick to tick through the

ovum, and the efficiency of ticks as vectors in nature—which is not known. Man is usually infected through contact with domestic animals, rarely by the bite of a tick, and man-to-man spread is rare but may occur through infected sputum.

ÖZBİL (p. 574) shows that *R. burneti* may be isolated from the urine of infected mice from 3 to 16 days after intraperitoneal inoculation, and that it may remain viable for 48 hours in urine at room temperature (whereas *R. prowazeki* and *R. mooseri* die in 60–90 minutes). Animals infected with Q fever are therefore likely to transmit infection by contaminating food and drink with urine, or by contaminating material which may subsequently be inhaled as dust (see also WIESMANN *et al.*, below).

The association of Q fever with animals, particularly sheep, is stressed by many authors. In Britain MARMION *et al.* (p. 983) found a relationship between the proportion of human reactors to the complement-fixation test (blood donors) and the density of the sheep population on the one hand and the consumption of raw cow's milk on the other. STOKER *et al.* (p. 171) isolated *R. burneti* from the placentas, and from perineal wool tags, of sheep, and STOKER and MARMION (p. 172) isolated it from *Haemaphysalis punctata* collected from sheep of the same flock. This was not a surface contamination from infected wool; the organism was in the ticks, but this does not necessarily mean that it is transmitted by ticks. Positive complement-fixation tests were found in sheep in Wales, where an outbreak in man was reported, though the organism was not isolated from the milk of ewes or from ticks (MONTHLY BULL. MINISTRY OF HEALTH AND PUBLIC HEALTH LAB. SERVICE, p. 570). In south-west Scotland, where the human infection is rare, GRIST (p. 1110) found only scanty infection in cattle and sheep.

In an outbreak in Switzerland most of the patients had been in contact with sheep, and *R. burneti* was isolated from the blood and urine of sheep; WIESMANN *et al.* (p. 571) remark that infective dried urine could be inhaled with dust (see also ÖZBİL, above).

In Slovakia where positive complement-fixation tests were found in a number of persons clinically suspected of the disease, most of the patients had been in contact with domestic animals, and BREZINA and TÁBORSKÁ (p. 1415) report that antibody has been found in deer, hares, foxes, rats, mice and shrews. *R. burneti* has been isolated from the liver and spleen of wild birds caught near a focus of Q fever in Czechoslovakia (SYRŮČEK *et al.*, p. 173), and from the liver and spleen of fowls inoculated with the organism (SYRŮČEK, p. 173).

COMBIESCU *et al.* (p. 43) describe an explosive outbreak of Q fever on a farm in Rumania, noting that though pulmonary lesions were the rule, there were cases in which *R. burneti* was found in the blood and in which pulmonary signs were absent. The source of infection was the animals which had aborted.

In abattoir workers in Algiers LACROIX *et al.* (p. 1110) found 14.6% positive to the complement-fixation test; 29.6% of sheep aged 6–12

months were also positive. MIMOUNE *et al.* (p. 738) report an outbreak in French soldiers in Algeria, who probably caught the infection through travelling in waggons previously used for sheep, and not properly cleaned.

In the Addis Ababa region of Ethiopia the rickettsial micro-agglutination test indicates that Q fever is common in cattle, sheep and (especially) goats, and in peasants and abattoir workers (GUTFREUND *et al.*, p. 572).

Q fever is the most common of the rickettsial fevers of southern Africa, most cases occurring in newcomers from north-west Europe; CRADDOCK and GEAR (p. 306) now report it from Kenya. The disease is associated with tick-infested cattle or sheep; and infection is acquired through inhalation of infected dust originating from dried discharges from these animals. BROTHERSTON and COOKE (p. 1111) report 4 human cases in Kenya, 3 of whom worked in contact with cattle. The authors conclude that many of the short-term fevers of East Africa may be Q fever. Positive complement-fixation tests for *R. burneti* were found in Kenya by BROWN (p. 1330) in sera from dogs, camels, goats and cattle, but not from horses. All were negative for *R. prowazeki*.

Q fever occurs in Lebanon, where GARABEDIAN *et al.* (p. 1329) found positive complement-fixation tests in up to 22% of the people tested; the rates in those exposed to domestic stock were higher. Milk from cattle and goats, but not from sheep, was infective to guineapigs, though the number of specimens from sheep was too small to be a valid test. The authors suspect that the widespread consumption of a mixture of raw meat and wheat may be one way in which the disease is spread. Complement-fixation tests were found positive for Q fever in adults (and a few children) in 3 villages in Persia (GADJUSEK and BAHMANYAR, p. 174).

Q fever is present in various parts of Central Asia, and CHUMAKOV (p. 305) reports that *R. burneti* has been isolated from *Hyalomma excavatum*, *Argas persicus* and certain mites. Infection is usually acquired by inhalation of infected dust, but the faeces of ticks, or dried remains of dead ticks, may be important in dust infection. Small outbreaks have occurred in the European part of the Soviet Union in workers handling cotton from Central Asia. ZHMAEVA *et al.* (p. 430) state that *R. burneti* has been found in various rodents of southern Soviet Central Asia, in sparrows, various ticks and mites. They recovered it from the brains of sparrow nestlings and from pools of mites and *Argas reflexus*. These ectoparasites may be implicated in transmission to man. ZEMSKAYA and PCHELKINA (p. 431) were able to transmit *R. burneti* through *Dermanyssus gallinae* and *Bdelonyssus bacoti*.

RIBEIRO DO VALLE *et al.* (p. 43) describe a case of Q fever in a stockman. This was stated to be the first case in Brazil in which serological evidence of the disease (complement-fixation test) has been found, but a serological study of meat handlers in São Paulo by BRANDÃO *et al.* (p. 1331) showed a few positive for Q fever; sera from cattle were also positive.

The first epidemic of Q fever to be reported from Vietnam is described by QUINTIN *et al.* (p. 174) who confirmed 25 cases in the crews of French

naval ships at Saigon. The origin of the outbreak could not be determined.

ORFEI (p. 1111) describes the development of *R. burneti* in the vitelline membrane of the chick embryo.

VICTOR *et al.* (p. 306) showed that guineapigs infected simultaneously with *Brucella suis* and *R. burneti* developed less severe infection than animals receiving the same doses separately. The explanation is not known; it is not likely to be the interference phenomenon. It may be important when inconsistencies arise in infection rates in groups of experimental animals.

PHILIP and WHITE (p. 42) recovered the rickettsia of Q fever and the agent of "maculatum disease" from ticks caught in part of Mississippi.

BLANC (p. 1189) isolated an organism resembling *R. burneti* from wild-caught *Hyalomma* in Morocco, and demonstrated it in up to 44% of rabbits. This organism produces transient fever, but without pulmonary involvement, in man. The rabbits were also infected with murine typhus.

Charles Wilcocks

MALARIA

In this section abstracts are arranged as far as possible in the following order:—Human malaria—epidemiology, aetiology, transmission, pathology, diagnosis, clinical findings, treatment, control; Animal malaria—monkeys, other animals, birds.

BHATIA, M. L., SATYA PRAKASH & RAMAKRISHNAN, S. P. **Malaria Vectors and some Epidemiological Features of Rajasthan.** *Bull. Nat. Soc. India for Malaria & other Mosquito-Borne Dis.* 1957, Mar., v. 5, No. 2, 100-109.

Two malaria reconnaissances in the Udaipur, Bharatpur and Jodhpur divisions of Rajasthan [once Rajputana] included records of the spleen and parasite rates, anopheline surveys, and general information. In the hill areas, including Udaipur, transmission is said to start in July and continue through winter to end in April, with peaks in October and March. Malaria is on the whole stable. In the plains transmission starts in July, reaches a peak in October, and ends in November; the disease is very unstable and has an epidemic cycle of 6 or 7 years. Sporozoites were found in one specimen of *Anopheles culicifacies* and one of *A. fluviatilis* which showed respectively anthropophilic indices of 50 and 38%, and both of which were numerous in Udaipur. An epidemic which was current in Bharatpur, necessitating emergency control, prevented all but observation of spleen and parasite rates which in children were 45 and 61%. Control had previously been practised in Jodhpur and anophelines were scanty. Malaria is here patchy in distribution because many of the waters are too saline to permit anopheline breeding. A final

statement gives the known anopheline fauna for each of the divisions of the State.

[The continuation of transmission throughout the winter in areas where the temperature falls markedly below normal transmission levels needs fuller verification.]

G. Macdonald

See also p. 1247, RAMACHANDRA RAO & RAJAGOPALAN, **Observations on Mosquitoes of Poona District, India, with special reference to their Distribution, Seasonal Prevalence and the Biology of Adults.**

BRUCE-CHWATT, L. J. & CHARLES, L. J. **First Field Trial of 377 C 54, a New Antimalarial Compound.** *Brit. Med. J.* 1957, July 6, 23-6, 1 graph.

An account is given of field trials carried out on African schoolchildren in Lagos, Nigeria with 377 C54 [2:5-bis (cyclo-hexylaminomethyl) naphthalene-1:6-diol dihydrochloride], recently synthesized in the laboratories of the Wellcome Foundation in London. This drug belongs to a series of mono- and dihydroxynaphthalenes, and has been shown to possess high activity against avian and simian plasmodia.

316 children were divided into 2 series of 3 groups and subjected to the following regimens: (1) single dosage at 300 mgm., 200 mgm. and 100 mgm. respectively, and (2) repeated dosage for 2 consecutive days at 300 mgm., 200 mgm. and 100 mgm. respectively. In addition a separate group were given a single dose of 100 mgm. of chloroquine; a small group of 20 children, given a placebo, served as a control.

Preliminary screening showed a spleen rate of 75.3%. *P. falciparum* was recorded in 72.8% of the blood smears, *P. malariae* in 25.1% and *P. ovale* in 2.1%.

In series 1 disappearance of asexual parasites was complete only for the 300 mgm. group. 88.6% of the 200 mgm. group were cleared, but only 47.7% of the 100 mgm. group. In series 2 all 3 regimens of 377 C54 produced total clearance, as did the single 100 mgm. dose of chloroquine. No change was noted in the control group.

Judged by the comparative clearance rate with single doses it appeared that 377 C54 is approximately one-half to one-third as active against *P. falciparum* as chloroquine. The fact that after 4 weeks there was no evidence of a significant decrease of the spleen rate or average enlarged spleen in any of the 6 groups on 377 C54 suggested that the action of the drug is not so complete as that of the 4-aminoquinolines given in single doses of 200 or 300 mgm.

The trials indicated that 377 C54 has a pronounced schizontocidal effect against *P. falciparum*, *P. malariae* and *P. ovale*. There was no evidence of any direct gametocytocidal or sporontocidal action on *P. falciparum*. The drug was well tolerated in a dosage of about 30 mgm. per kgm. given over 2 days.

G. Covell

DAVIS, M. J. & VANDER PLOEG, D. E. **Acute Porphyria and Coproporphyrinuria following Chloroquine Therapy. A Report of Two Cases.** *Arch. Dermat.* 1957, June, v. 75, No. 6, 796-800. [17 refs.]

"Two patients are reported who developed toxic reactions shortly following chloroquine therapy. Chloroquine in one patient caused abdominal symptoms, hepatic dysfunction and increased urinary excretion of uroporphyrins, coproporphyrins, and porphobilinogen, and in another patient caused abdominal symptoms and increased excretion of coproporphyrins. These changes were apparently reversible after the drug was discontinued. A brief review of chloroquine toxicity is presented."

[See this *Bulletin*, 1957, v. 54, 786.]

MATHURIN, L. Deux cas d'intoxication mortelle de petits enfants par Malocide et Optalidon. [**Two Cases of Fatal Poisoning of Small Children by Malocide and Optalidon**] *Méd. Trop.* Marseilles. 1957, Jan.-Feb., v. 17, No. 1, 122-4.

The case of immediate interest to readers of this *Bulletin* is that concerned with fatal poisoning with Malocide [pyrimethamine].

A child of 3 gained access, while her parents were asleep, to a container of Malocide and consumed what was estimated to have been 20 to 30 tablets. The child died after the usual distressing symptoms within 4 to 5 hours, despite all efforts to save her.

[No less than 8 cases of accidental poisoning of small children by pyrimethamine have been reported in this *Bulletin* in the last 2 years alone (1955, v. 52, 507; 1957, v. 54, 264, 923). There can be no justification for leaving such dangerous drugs where young children can easily obtain them, when these tragic fatalities can usually be prevented by means of elementary precautions.] *H. J. O'D. Burke-Gaffney*

CLYDE, D. F. **An Examination of Factors Involved in the Transfer of Pyrimethamine in Human Milk.** *East African Med. J.* 1957, Mar., v. 34, No. 3, 81-5.

In a previous paper [this *Bulletin*, 1957, v. 54, 392] the author and his colleagues showed that pyrimethamine administered to a nursing mother is excreted in the milk in sufficient quantity to eliminate parasitaemia in infants suffering from malaria. It was concluded, however, that for various reasons the method was not satisfactory for the treatment of malaria in infants.

In the work reported in the paper under review the author has attempted to assess the value of the method in prophylaxis. It was found that after a single dose of 50 or 75 mgm. of pyrimethamine ingested by the mother the quantity of the drug appearing in the milk over a 2-day period was nearly twice that required for the cure of malaria by direct treatment

of the baby. There are, however, certain disadvantages in the use of this method for prophylaxis:

(1) there is a risk of resistance to pyrimethamine being produced by the ingestion of very low doses by the infant spread over a number of days;

(2) in most cases it is as easy to treat mothers and babies directly as to treat mothers alone;

(3) the greater amount of the drug which must be used for indirect as compared with direct treatment of the baby increases the cost.

The conclusion reached is that for prophylaxis of malaria the method of indirect administration of pyrimethamine to infants through maternal milk is more costly and no more efficient than administration of the drug to mother and baby individually.

G. Covell

WILSON, T. & EDESON, J. F. B. **Studies on the Chemotherapy of Malaria. VI. The Role of Suppressive Drugs in Malaria Control in Malaya.** *Med. J. Malaya*. 1957, Mar., v. 11, No. 3, 190-200. [22 refs.]

The review of factors influencing the choice of a control method contained in this paper is of interest not only to workers in Malaya but also to those connected with antimalaria campaigns in other parts of the world.

In Malaya, antilarval measures are preferred for urban areas. In rural areas where homesteads are scattered, house-spraying with residual insecticides is the method of choice. In villages, estates and mines the choice of method is largely governed by local circumstances, such as the presence or absence of other protected areas nearby and the amount of population movement. In general, antimosquito measures are used wherever possible, reinforced where necessary by suppressive therapy. For visitors to malarious areas drug suppression is the most effective weapon for ensuring freedom from malaria and the authors point out that this can be practically guaranteed for any intelligent person and his family at a cost not exceeding the price of 100 cigarettes per annum.

The relative values of amodiaquine, chloroquine, mepacrine, proguanil and pyrimethamine for the suppression of malaria are discussed. Suggestions are made for the dosage of each drug and an estimate is given of the annual cost per adult thus protected.

G. Covell

CLYDE, D. F. & KINGAZI, H. **Diethyl Toluamide as a Mosquito Repellent.** *East African Med. J.* 1957, May, v. 34, No. 5, 185-9, 1 graph.

The new insect repellent diethyl toluamide has been tested in Tanganyika against *Anopheles gambiae* and *Culex fatigans*, by the exposure of treated arms in cages of artificially reared mosquitoes. It was found that the duration of complete protection, under the conditions

prevailing (which did not cause excessive sweating) was generally 18 to 20 hours. Comparative figures for a cream containing 40% of dimethyl phthalate were 4 to 4½ hours.

J. R. Busvine

DHIR, S. L. & AMRIK SINGH. **Field Studies on the Comparative Residual Effectiveness of DDT and Dieldrin against Anopheline Mosquitoes.** *Bull. Nat. Soc. India for Malaria & other Mosquito-Borne Dis.* 1957, Mar., v. 5, No. 2, 110-16, 2 figs. (1 folding).

An effort was made by field trials to compare the efficacy of 3 preparations, all wettable powders—50% dieldrin imported, 75% DDT imported, and 50% DDT manufactured in India. Dieldrin was applied at 25 mgm per square foot and DDT at 100 mgm. per square foot. These were to be applied in 3 groups of villages while a fourth group remained untreated as a control. However, the treated and control villages were not comparable, insecticides having been applied twice a year since 1947 in the treated villages and never in the controls.

Daily estimates of anopheline density revealed a significant increase in the seventh week in the area treated with dieldrin, in the fifth week in that treated with 75% DDT, and in the fourth week in the other. Findings are recorded in terms of gross anopheline catch, the commonest mosquito being *Anopheles subpictus* which is known to be resistant to DDT in a nearby area and may be resistant here. Interpretation of the findings is therefore very difficult indeed.

G. Macdonald

JONES, J. C. **A New Standard for the Rapid Detection of DDT Tolerance in *Anopheles quadrimaculatus* Larvae and Pupae.** *Mosquito News.* 1957, Mar., v. 17, No. 1, 1-9.

The levels of tolerance to DDT in the larvae and pupae of known sexes, stadial ages and nutritional and rearing status have been determined in a susceptible strain of *Anopheles quadrimaculatus*. The test method involved the exposure of the insects to a very high concentration of DDT, viz., 100 p.p.m. for short periods, ranging from 1 to 75 minutes for larvae, and 30 to 360 minutes for pupae. After exposure the insects were rinsed in distilled water and their condition was checked every 2 hours until they died, pupated or emerged into adults. Median lethal times were calculated.

The experiments revealed that the sex of the larvae does not significantly affect the tests, that DDT tolerance is lowest soon after moult and that the tolerance to DDT increases during the fourth stage. Newly metamorphosed pupae are twice as tolerant to DDT as the most resistant larvae; significant sexual differences in DDT tolerance appear first in the pupal stage; female pupae being more tolerant.

The author believes that the exposure test is rapid, easy to perform and requires a minimum of equipment. The test may also be used to provide

laboratory standards of considerably wider range and greater accuracy than are now available with continuous exposure testing methods.

W. Z. Coker

PESQUEIRA, M. E. Programa para la erradicación del paludismo en México. [**Programme for Eradication of Malaria in Mexico**] *Bol. Epidemiológico*. Mexico. 1956, Jan., Feb. & Mar., v. 20, No. 1, 10-17, 9 figs. Also in *Bol. Oficina Sanitaria Panamericana*, 1957, June, v. 42, No. 6, 537-47.

The XIV Panamerican Sanitary Conference at Santiago, Chile, in October 1954 recommended as a matter of urgency the eradication of malaria from the American Continent [this *Bulletin*, 1956, v. 53, 282, 283]. At the VIII World Health Assembly in Mexico City the following May, the Republic of Mexico agreed to the proposition and in November a decree was passed announcing the intention to implement it. Hitherto Mexico had exercised partial control methods which did not cover the whole malarious area of the country.

Mexico has a diverse climate, varying from the temperate to the tropical and with dry and rainy areas. In general the warm regions are in the south and on the coast and the temperate in the north and the plateaux. The malarious area covers almost three-quarters of the country and more than 16 million persons are exposed to infection [*ibid.*, 1957, v. 54, 395]. The greatest intensity is in the States of the Isthmus of Tehuantepec. Malaria occupies the third place as a cause of death, being exceeded only by gastroenteritis and pneumonia. The average mortality per 100,000 is 89.9 and varies from 0.8 in the Federal District to 449.2 in Oaxaca. The mortality for each State and Territory is shown in a table. It is estimated that there are 2 million cases of malaria and 25,000 deaths every year, and although the death rate has tended to decrease slightly in recent years this may partly be accounted for by a general improvement in living conditions.

There are 25 species and 1 variety of *Anopheles* known in Mexico. Most of these play a small part as secondary vectors of malaria and the principal carriers are *Anopheles pseudopunctipennis pseudopunctipennis* and *A. albimanus*: the first is widespread throughout the malarious area and the second is found on the coast and in the adjoining plains. All 3 principal species of *Plasmodium* occur, but in nearly 5,000 positive blood films from children in 1947-1955, *P. vivax* accounted for 88.3%, the remainder being *P. falciparum*, *P. malariae* or mixed infections.

The Government of Mexico has obtained the cooperation of UNICEF which is to provide equipment and insecticides, and of WHO which is to give technical assistance.

The organization of the National Commission for the Eradication of Malaria is described in detail. It follows the now established pattern [*ibid.*, 1957, v. 54, 1049], namely, stages of preparation, attack, consolidation and surveillance. It is planned that the campaign should

occupy 8 years, 4 of which will be devoted to actual domiciliary spraying with DDT and dieldrin. Chemoprophylaxis and chemotherapy will play an important part in dealing with extradomiciliary transmission, and the need for cooperation by doctors, medical institutions and the public in detecting and treating isolated cases is stressed.

Eradication will be regarded as complete if no new primary autochthonous cases of malaria are found as a result of careful search for 3 consecutive years after spraying has been interrupted.

H. J. O'D. Burke-Gaffney

PASTACALDI, V., SAUTET, J. & VUILLET, J. Action de l'alcool, du vin et du vin sans alcool sur les traitements des affections à *Plasmodium berghei* chez la souris. [**Effect of Alcohol, Wine and Wine without Alcohol on Treatment of *Plasmodium berghei* Infections in Mice**] *Ann. Parasit. Humaine et Comparée*. 1957, Jan.-Mar., v. 32, Nos. 1/2, 9-20, 2 graphs. [11 refs.]

The authors have extended their studies [see this *Bulletin*, 1956, v. 53, 863] on the effect of adding red wine to the diet of mice suffering from *Plasmodium berghei* malaria. In the new experiments they used 130 mice on a red wine diet, 130 mice on red wine minus alcohol, 130 mice on alcohol, and 10 controls. 17 days later they were inoculated with a standard quantity of *P. berghei*. The following day Nivaquine [chloroquine] in 2 doses (30 and 90 mgm. per kgm.) and quinacrine [mepacrine] (46 and 138 mgm. per kgm.) were given and were continued for 5 days. The weight of the mice, degree of parasitaemia and mortality were then studied.

The results showed that with the smaller doses of the drugs, alcohol alone or as contained in red wine improved the action of the drugs in all three respects; but in combination with higher doses, an increased mortality (in the absence of parasitaemia) was the result. In other words, the toxicity of both drugs was greater in mice with an alcoholic background.

P. C. C. Garnham

SAUTET, J., VUILLET, J., ARNAUD, G. & AUSSEIL, M. Action comparée de diverses huiles de foie de morue et de solutions de vitamines A et D comme modificateurs rapides du terrain dans les affections à *Plasmodium berghei*, chez la souris, traitées par des antimalariques à doses massives. Note I. [**Comparison of the Influence of Different Samples of Cod-Liver Oil and of Solutions of Vitamins A and D on *P. berghei* Infections in Mice treated with Large Doses of Antimalarials**] *Bull. Soc. Path. Exot.* 1957, Jan.-Feb., v. 50, No. 1, 39-43, 1 chart.

_____, _____ & _____. Effets de l'adjonction immédiate d'huile de foie de morue ou de vitamine D et phosphate bicalcique

aux produits antimalariques utilisés dans le traitement des affections à *Plasmodium berghei*. Note II. [**Effect of Addition of Cod-Liver Oil or of Vitamin D and Calcium Phosphate at the Same Time as Drugs used in Treatment of *P. berghei* Infections**] *Ibid.*, 44-9, 4 charts.

—, DESANTI, E., VUILLET, J., ARNAUD, G. & AUSSEIL, M. Précisions sur l'adjuvant renforceur de terrain le plus favorable dans les traitements courts et à faibles doses par un amino-4-quinoléine (Chloroquine ou Nivaquine) dans les affections à *Plasmodium berghei* chez la souris blanche. Note III. [**Substances with Favourable Effect in Short Course of Treatment with Small Doses of a 4-aminoquinoline (Chloroquine, Nivaquine) in *P. berghei* Infections of the Mouse**] *Ibid.*, 49-59, 2 charts.

The effect of different diets on the course of *P. berghei* infection in mice has already been reported by these authors [this *Bulletin*, 1956, v. 53, 155, 156], and also the manner in which treatment by various drugs was affected under these conditions. As before mice were kept on a series of varied diets for 10 days before inoculation with *P. berghei*. 2 days later drug treatment was started and continued for 5 days, and the same diet was used for 28 days while observations continued for 52 days. The survival rate in mice receiving cod-liver oil, especially if not refined, was higher than in those receiving vitamins A and D in comparable quantities. Adjuvants to the bread and water diet of vitamins or cod liver was beneficial in treatment with nivaquine.

In a further series of experiments treatment with vitamins or cod-liver oil was started at the same time as drug treatment. It was continued for a period of 5 days with oral quinine, quinacrine [mepacrine], nivaquine [chloroquine] or malocide [pyrimethamine]. The adjuvants mentioned above appeared to aid treatment with quinine but not in the case of the synthetic antimalarials except possibly nivaquine.

In a third series of experiments with 465 mice an attempt has been made to define the best dosage and time for administration of adjuvants such as cod-liver oil or vitamins A and D. The composition and dosage of these substances are indicated. Oral treatment with small doses of drug comparable to those used in treatment of human patients was continued for 5 days. The results are set out in 3 tables indicating the effect on weight and mortality of the host and on parasitaemia. [The abstracter finds it difficult to come to any conclusion from these experiments.]

J. D. Fulton

HUFF, C. G. **Organ and Tissue Distribution of the Exoerythrocytic Stages of Various Avian Malarial Parasites.** *Exper. Parasit.* New York. 1957, Mar., v. 6, No. 2, 143-62. [21 refs.]

The incidence of exoerythrocytic stages of various malaria parasites in different avian hosts was determined in relation to blood or sporozoite

infection, and to the varying parasite-host combinations. The material was taken at different intervals after infection and is referred to in two main groups:— early (3–9 days) and late (10–19 days); the observations were carried out on sections of organs prepared in the usual way. 34 combinations were studied, involving *Plasmodium cathemerium*, *circumflexum*, *fallax*, *gallinaceum*, *lophurae*, *relictum* and *elongatum*, in canaries, chickens (and embryos), ducks (and embryos), partridges, pheasants, pigeons, quail and turkeys. *P. elongatum*, as was expected, behaved in a fashion of its own, and did not contribute to the overall pattern. Incidentally the gosling embryo was found to be a good host for this species in which, by the 6th day, exoerythrocytic stages became generalized. [No consideration is given here to the cryptozoic and meta-cryptozoic (= pre-erythrocytic) stages of any of the parasites.]

The general picture is provided by the behaviour of *P. gallinaceum* in chickens or *P. fallax* in turkeys: exoerythrocytic schizogony takes place in the capillary endothelium and lymphoid macrophage system in the early stages of sporozoite-induced infections, but in the later stages of blood-induced infections, where as a whole it is less prolific; it is, however, the inter-reaction of host and parasite which determines the exact pattern. Where the combination is less natural, sparse or degenerate parasites are found in both early and late infections, while in even more unsuitable hosts, exoerythrocytic stages are entirely lacking, as in the following: sporozoite-induced *P. gallinaceum* in partridges, sporozoite and blood-induced *fallax* in pigeons and pheasants, and blood-induced *fallax* in canaries, *lophurae* in chicks and *circumflexum* in canaries.

P. fallax has the widest range of infectivity in different hosts, in the following order of susceptibility:— turkey, partridge, chicken, quail, guinea-fowl, pheasant, canary, pigeon and duckling. This range is almost as extensive as that exhibited by *P. pinottii* of the Brazilian toucan (these two parasites are confirmed as being morphologically distinct). *P. lophurae* behaves much like *P. fallax* in regard to the incidence of exoerythrocytic schizogony; and this similarity is regarded as suggesting a close zoological relationship between the 2 species.

For detailed observations, including the involvement of particular organs, the reader is referred to the original article. *P. C. C. Garnham*

TAYLOR, Angela E. R. **The Effect of Paraminobenzoic Acid, Parahydroxybenzoic Acid and Riboflavin on *Plasmodium gallinaceum* in Chicks.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1957, May, v. 51, No. 3, 241–7, 4 figs. [11 refs.]

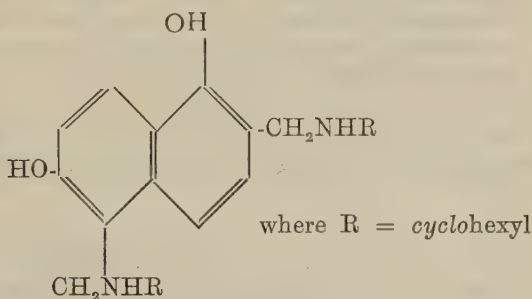
Similar experiments to those described here have already been reported in the case of *P. gallinaceum* with *p*-aminobenzoic acid and riboflavin [this *Bulletin*, 1957, v. 54, 399, 535]. *P*-hydroxybenzoic acid has been used in the same way with other malaria parasites [*ibid.*, 1954, v. 51, 468]. Addition of the benzoic acid derivatives to a basal diet were found

to cause an increase in parasitaemia, and deficiency of riboflavin lowered parasitaemia.

J. D. Fulton

DUFFIN, W. M. & ROLLO, I. M. **Antimalarial Activity of Hydroxy-Substituted Naphthalene Compounds.** *Brit. J. Pharmacol. & Chemotherapy*. 1957, June, v. 12, No. 2, 171-5.

When it was found that mono- and dihydroxy-substituted naphthalenes were active against *P. gallinaceum* infections in chicks a member of the series 377C54, with notable activity, namely 1:6-dihydroxy-2:5-bis (cyclohexylaminomethyl)naphthalene



was more extensively tested against a number of malarial infections. The methods of test used in *P. gallinaceum* infections were those described [this *Bulletin*, 1951, v. 48, 872]. Tests were also made on *P. berghei* infections in mice and on *P. cathemerium* infections in canaries, as well as against *P. knowlesi* in the rhesus monkey. Attempts to produce resistance to 377C54 in chicks were not successful.

The general method of estimation of these compounds was by extraction from tissues with ether at pH 8, then transfer to N/10-HCl followed by coupling with diazotized *p*-nitroaniline. The intensity of the resulting colour was measured at 465 mμ in a spectrophotometer. The results obtained on varying the character of the substituent groups in 1- and 2-hydroxy naphthalenes are described.

The marked activity against the chick infection by 377C54 was also observed against the other malarial species. Its action was rapid, and parasitocidal activity in treated hosts persisted for some time. Estimations showed that the substance was present only in liver and lung after 24 hours and persisted in these organs for some days. In the blood of human volunteers who received 600 mgm. of 377C54 orally a peak concentration was reached in about 2 hours and none was detectable in urine. In man it also appears to be retained in liver and lung. Pharmacological investigations showed that 377C54 in certain doses caused a marked fall in blood pressure in the cat. On plain muscle it had relatively little effect. Other pharmacological properties of the drug are outlined.

J. D. Fulton

See also p. 1248, MOUCHET *et al.*, Observations sur la biologie d'*Anopheles smithi* var. *rageaui* Mattingly et Adam 1954, vecteur d'un *Plasmodium* de mammifère aux environs de Yaoundé (Sud-Cameroun). [The Biology of *A. smithi* var. *rageaui*, a Vector of a Mammalian *Plasmodium* around Yaoundé]

TRYPANOSOMIASIS

In this section abstracts are arranged as far as possible in the following order:—African—human, animal; American—Chagas's disease and other trypanosome infections. In each form the following order is followed:—epidemiology, aetiology, transmission, pathology, diagnosis, clinical findings, treatment, control.

See also p. 1261, EAST AFRICA HIGH COMMISSION. **East African Trypanosomiasis Research Organization. Annual Report 1955-56.**

NIGERIA, NORTHERN. Med. Dept. **Sleeping Sickness Service Annual Report, 1st January, 1956-31st December, 1956.** 24 mimeographed pp. 1957: Kaduna.

During the year reviewed 1,833,362 people were examined and a sleeping sickness incidence of 0.15% is recorded. This is the lowest infection rate reported in Nigeria and is a significant reduction on the raised incidence of 0.23% found in 1955 [this *Bulletin*, 1956, v. 53, 294]. The 1956 figure is, however, biased by surveys in areas of low endemicity which had not been examined for many years. Excluding these, a more representative incidence of 0.18% is disclosed which is still the lowest level reached. Cases found on voluntary attendance at medical institutions exceeded those detected at resurvey, an indication of the value of sleeping sickness dispensaries. Cases discovered, however, at resurvey included a larger proportion of symptomless early cases, 91.5% compared with 63.0% among those attending voluntarily, while the latter category included a higher proportion of relapse cases. The dispensaries and resurveys appear to be complementary, and both are necessary. In the various Provinces the situation was generally satisfactory. In the Plateau Province pentamidine prophylaxis had to be reintroduced because after its cessation the infection rate rose rapidly to 2.4%; the incidence subsequently dropped to 0.27%. Chemoprophylaxis was employed in an important focus in the Ndzorov clan; 83.0% of over 20,000 inhabitants (belonging to this and other clans) received pentamidine and the result was to be assessed early in 1957 at the time the second injection was due.

In an attempt to solve the problem of trypanamide resistance Melarsen has been employed in relapse cases and a reduction of 5.9% in the

relapse rate is reported. It is not clear that this decrease is due to the drug because the relapse rate was unchanged in the area where the problem was greatest.

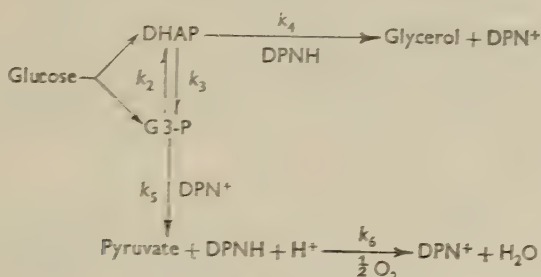
A small experiment has shown that the cost of bush clearance by mechanical saws is slightly lower than by hand labour alone and less labour is needed. The insecticide trials previously reported have been continued. A small population of tsetse has either survived or reinvaded an 8-mile stretch of river sprayed with water-dispersible DDT powder in 1955. Trials of arboricides are proceeding but results cannot be assessed yet.

The report ends with a series of appendices in which the year's results are tabulated.

T. H. Davey

GRANT, P. T. & FULTON, J. D. **The Catabolism of Glucose by Strains of *Trypanosoma rhodesiense*.** *Biochem. J.* 1957, June, v. 66, No. 2, 242-50, 3 figs. [37 refs.]

T. rhodesiense requires great quantities of glucose, by the catabolism of which it obtains its energy. The chemical processes involved were investigated by using glucose containing radio-active carbon. Under aerobic conditions pyruvate, and to a less extent glycerol, were the main end products. Under anaerobic conditions, equal quantities of pyruvate and glycerol were formed. Apparently the glucose is catabolized according to the Embden-Meyerhof-Parnas scheme.



DHAP = dihydroxyacetone phosphate

G 3-P = glyceraldehyde 3-phosphate

DPN⁺ = diphosphopyridine nucleotide, oxidized

DPNH = " " reduced

K₁, K₂, etc. refer to the velocities of the different reactions.

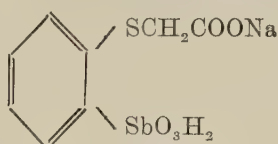
Rats infected with trypanosomes have abnormally high levels of pyruvate in the blood: when the animals are treated with a trypanocidal drug the pyruvate level rapidly falls. Apparently the trypanosomes form pyruvate more rapidly than the host can metabolize or excrete it.

[This is an important but highly technical paper, and the original should be consulted by those interested in the metabolism of trypanosomes.]

F. Hawking

PAGCHANIAN, A. **Chemotherapy of African Sleeping Sickness. III. Chemotherapy of Experimental *Trypanosoma gambiense* and *Trypanosoma rhodesiense* Infections in Mice with Captostibone.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1957, May, v. 51, No. 3, 257-64.

Captostibone (sodium 2-(carboxymethylmercapto) benzene stibonate) is a new antimonial developed by Hoffman-La Roche Inc.



The intraperitoneal LD50 for mice is about 300 mgm./kgm. and the maximum tolerated dose about 250 mgm./kgm. The drug is poorly absorbed from the alimentary canal. In intraperitoneal doses of 50-250 mgm./kgm. daily for 5-42 days it suppressed *Trypanosoma cruzi* infections in mice but did not cure them. The intraperitoneal administration of 150-200 mgm./kgm. daily for 4 days cured 80-100% of mice infected with old laboratory strains of *T. gambiense* or *T. rhodesiense*. Trypanosomes disappeared from the blood within 24 hours of treatment.

This compound has also been used to treat a few human patients suffering from leishmaniasis and the results are said to be encouraging. Administration of 1.6 to 7 mgm./kgm. intramuscularly every other day for 10 days (total 3 gm. for an adult patient) caused no toxic effects apart from a burning sensation at the site of injection and (in a few cases) reversible icterus and renal irritation.

[Many other compounds are known which are much more active than Captostibone in curing laboratory infections of trypanosomiasis.]

[For Parts I and II in this series, see this *Bulletin*, 1956, v. 53, 31; 1957, v. 54, 542.]

F. Hawking

THILLET, C. J., Jr. & CHANDLER, A. C. **Immunization against *Trypanosoma lewisi* in Rats by Injections of Metabolic Products.** *Science.* 1957, Feb. 22, v. 125, 346-7.

Rats were infected with *T. lewisi* and were killed during the phase of development of the infection "before any demonstrable ablastin had formed".

The trypanosomes were separated from the blood and incubated in equal parts of saline and normal rat serum for 24 hours at 27.5°C. at a concentration of 200 million parasites per ml. of medium. The trypanosomes maintained their numbers and motility. The medium was then separated from the trypanosomes which were disintegrated by repeated freezing and thawing.

The trypanosome-free medium and the trypanosome bodies were then injected respectively into 2 groups of rats; 6 injections were given at

3-day intervals and 10–12 days later the 2 groups, together with the control rats, were challenged by infection with *T. lewisi*. The control rats took a normal infection. The rats that had received trypanosome bodies took a lower grade of infection which was apparently of short duration and the rats which had received the trypanosome-free medium did not become infected. In addition the serum from rats which had received the trypanosome-free medium contained agglutinins against *T. lewisi* active at a titre of 1 in 200, more active than the serum of rats that had recovered from a normal infection.

The authors conclude that ablastic activity may be developed against metabolic products of the trypanosomes rather than the trypanosomes themselves.

[The abstracter has attempted to repeat these experiments but has found the experimental details inadequate.] W. E. Ormerod

NÁQUIRA, F. & NEGhme, A. Contribución al estudio de la enfermedad de Chagas. III. Encuesta epidemiológica en algunas localidades del Departamento de Arica (Provincia de Tarapacá, Chile). [**Contribution to the Study of Chagas's Disease. III. Epidemiological Survey of some Localities of the Department of Arica (Tarapacá, Chile).** *Bol. Chileno de Parasit.* 1957, Apr.–June, v. 12, No. 2, 22–3.

The English summary appended to the paper is as follows:—

“ 1.—Human cases of Chagas' disease have been found in two endemic areas where *T. infestans* was ten years ago eradicated.

“ 2.—Xenodiagnosis performed in 63 individuals above 12 years of age was positive in eleven cases (17·4%) while the complement-fixation test was positive in 20 of 43 individuals (46·4%).

“ 3.—It was not possible to capture *T. infestans* specimens in either localities.”

[The authors remark that they could not exclude the possibility that these infected persons might have been in contact with triatomids in neighbouring, uncleared, areas.]

PICK, F. Sur un dispositif d'alimentation de réduvidés hématophages pour la recherche indirecte de formes métacycliques du *Trypanosoma cruzi*. [**A Feeding Device for Triatomids for the Indirect Study of Metacyclic Forms of *Trypanosoma cruzi***] *Bull. Soc. Path. Exot.* 1957, Mar.–Apr., v. 50, No. 2, 220–21.

The author describes a modified and much improved apparatus for the feeding of Triatominae so as to collect the faeces for determining the presence of metacyclic *T. cruzi*.

A double-ended cone is constructed of a material to which the bugs are able to cling [rough-surfaced card would presumably be suitable]. The

height of the cone is 10 cm., and the diameters of its apertures are 3 and 7.5 cm., respectively. The smaller (upper) aperture is closed by a layer of close-meshed gauze, through which feeding can take place upwards onto the ventral surface of a blood-donor animal. Triatomids for testing are enclosed in the cone, either before or after feeding, and the device is placed with its large aperture standing in a Petri dish of suitable dimensions. The faeces drop downwards and may subsequently be examined or inoculated into test animals.

[A number of devices based upon the same principle have been previously described. In the abstracter's opinion the present modification is the best to date, possessing the virtue of simplicity both in construction and in use.]

N. R. Phillips

PICK, F. Sur des conditions extérieures de la cristallisation réduvidique de l'hémoglobine: la prise du repas sanguin des réduvidés hématophages sur des volontaires alités et sur des animaux curarisés. [**External Conditions in the Crystallization of Haemoglobin by Triatomids: The Blood Meal Taken on Volunteers Lying in Bed and on Curarized Animals**] *Bull. Soc. Path. Exot.* 1957, Mar.-Apr., v. 50, No. 2, 234-6, 2 figs. on pl.

The feeding of triatomid bugs on or about the face of human beings is well known. In two experiments, the feeding habits of nymphs and adults of *Panstrongylus megistus* and *Triatoma infestans* were investigated under conditions of unrestricted movement by the bugs.

When allowed to feed upon animals anaesthetized by curare, the bugs fed indiscriminately as to site, taking the shortest distance to the host and only rarely making contact other than by the mouthparts. With human volunteers, who were lying in beds with only the left forearm and face exposed, bugs were dropped on to the bedclothes from a height of 1½ metres. Initial attempts to feed were made at the site of alighting, but feeding was eventually achieved only at the exposed parts of the body. It is concluded that the apparent preference of bugs to feed upon the face is, in fact, a matter of accessibility.

No difference was observed in the pattern of crystallization of haemoglobin by bugs which had fed upon different parts of the body.

N. R. Phillips

LEISHMANIASIS

In this section abstracts are arranged as far as possible in the following order:—visceral, cutaneous, muco-cutaneous.

HEISCH, R. B. **The Isolation of *Leishmania* from a Ground Squirrel in Kenya.** *East African Med. J.* 1957, May, v. 34, No. 5, 183.

There have been 2 outbreaks of kala azar in Kenya in recent years [this *Bulletin*, 1955, v. 52, 520; 1956, v. 53, 979]. From one of the areas, Marigat, a ground squirrel *Xerus rutilus* was caught and a hamster was inoculated with its emulsified spleen. A year later the hamster's spleen was found to be very enlarged and contained numerous leishmaniae resembling *L. donovani*. Direct examination of ground squirrels from infected areas has always proved negative and it is presumed that the infections are inapparent, a not unusual finding in primary vertebrate hosts of zoonoses. It is hoped to test at least another 100 ground squirrels by inoculation of hamsters with their spleens.

Lizards in the kala azar area are also infected with leishmaniae, but these are not pathogenic for hamsters. *H. J. O'D. Burke-Gaffney*

FEVERS OF THE TYPHUS GROUP

In this section abstracts are arranged as far as possible in the following order:—general; louse-borne typhus, flea-borne typhus, mite-borne typhus; rickettsialpox; tick-borne typhus; Q fever, other rickettsial diseases.

WOJCIECHOWSKI, E., LEWIŃSKA, Zofia & MIKOŁAJCZYK, E., with the technical assistance of Apolonia PRZYBYŁA. Przetrwanie zarazka duru wysypkowego w narządach gryzoni zakażonych doświadczalnie. [The Persistence of Typhus Rickettsiae in the Organs of Experimentally Infected Rodents] *Przegląd Epidemiol.* Warsaw. 1957, v. 11, No. 1, 39-46. [17 refs.] English summary.

A study has been made of the persistence of *Rickettsia prowazeki* in the organs of experimentally infected wild and laboratory rodents. The animals were inoculated intraperitoneally with a suspension of infected louse gut, and the presence of rickettsiae was determined by the inoculation of guineapigs and lice with suspensions of organs removed at intervals after infection. In guineapigs rickettsiae were recovered from the brain after 16-20 days, from the spleen after 16-19 days, from the adrenals after 16 days, and from the bone-marrow after 16-19 days. Similar figures were obtained in experiments with white rats, white mice, wild rats and bank voles (*Microtus arvalis*), and the detailed results are presented in a table.

D. J. Bauer

See also p. 1255, AUDY, **Malayan Trombiculid Mites. 2. Naked-Eye Observations on Attached Chiggers, with a Simple Checklist of Malayan Species, and Details of Preferred Hosts.**

AUDY, J. R. **Trombiculid Mites infesting Birds, Reptiles, and Arthropods in Malaya, with a Taxonomic Revision, and Descriptions of a New Genus, Two New Subgenera, and Six New Species.** Reprinted from *Bull. Raffles Museum*. Singapore. 1956, Dec., No. 28, 27-80, 10 figs. [40 refs.]

This is a paper to be consulted by specialists in the systematics of trombiculid mites. The genus *Siseca* is created and contains 4 species of which *S. subrara* is new and parasitic on pill-millipedes. *Eltonella* is a new subgenus in the genus *Eutrombicula*, there being 2 new species *Eu. (E.) eltoni* from scorpions and *Eu. (E.) tweediei* from flying lizards. Other new species are *Eutrombicula fieldi* from a skink and flying lizards, *Babiangia booliati* from skinks and *Fonsecia celesteae* from snake and skink. Certain bird-chiggers are grouped in a new subgenus *Vorcana* of the genus *Trombicula*.

These new groupings and the new species are fully defined and described with figures. A key is given to genera and groups and there are also notes on taxonomic points and host records. Occasionally trombiculids occur as accidental stragglers on unlikely hosts. Instances are given and a plea made for discrimination in the way such events are recorded in checklists. It is within the scope of this paper to emphasize that the scrub typhus vectors, *T. deliensis* and *T. akamushi*, although essentially mammal parasites, do occur on ground birds such as quail. *T. akamushi* occurs in greater numbers on quail than on its usual host, field rats, in Malayan grasslands, but *T. deliensis* has a wider host range and is less numerous on ground birds.

D. S. Bertram

AUDY, J. R. **Laurentella, a New Subgenus of Trombiculid Mites, with Notes on Biology and Medical Importance.** Reprinted from *Bull. Raffles Museum*. Singapore. 1956, Dec., No. 28, 5-26, 1 fig. [Numerous refs.]

This new subgenus, *Laurentella*, of 22 species distributed mainly in the Oriental and Australasian region includes the "indica-group", "debilis-group" and other trombiculids. *Euschöngastia (Laurentella) indica* is a widespread species common on commensal rats in urban areas and *E. (L.) audyi* is dominant on tree-living mammals of Malaya and Borneo. Both species are possibly vectors of rickettsiae among their animal hosts. Synonymy, previous and new records, taxonomic and distributional points are discussed for these and several other species. Other species still await formal description. Notes are given on biology and hosts. In

general, the free-living stages of mites of this subgenus infest the nests of the host, or nearby, and there is some tendency for a close host-specificity to develop.

D. S. Bertram

HARRISON, J. L. **The Effect of Withdrawal of the Host on Populations of Trombiculid Mites.** Reprinted from *Bull. Raffles Museum*. Singapore. 1956, Dec., No. 28, 112-19.

"1. It is sometimes assumed that the removal of rats from an area infected with mite-typhus (scrub-typhus) will help to control the disease. Since the number of chiggers (mite-larvae) available depends upon the number of rats three months or more before, this seems unlikely.

"2. A serious possibility, however, is that removal of rats may actually increase the risk by increasing the unattached chiggers available.

"3. To test this, marked rats, frequently retrapped, were detained before release for one or two nights, and their infestations compared with those released the same day, or detained for only one night.

"4. The numbers of *Trombicula akamushi* or *deliensis* on a rat are positively correlated with the number on the same rat at an earlier recapture. This fact is used as a standard against which to measure the number of chiggers found. The total numbers on all the rats undergoing any one treatment are expressed as a percentage of the number at first capture. When like conditions are compared, the numbers on rats detained are greater than the numbers on rats which had not been detained, and the numbers on rats detained for two days are at least twice as great as the numbers on rats detained for one day only.

"5. The explanation proposed is that a rat, by repeatedly returning engorged chiggers to its own range, establishes a self-infestation. If the rat is not in its usual haunts the chiggers which hatch out in its absence, accumulate on or near the surface of the soil until either the rat returns, or a chance host (possibly a man) appears.

"6. The mere removal of rats from a typhus-infected locality will, therefore, produce an immediate increase in the risk of typhus. The longer the life of a free-living unfed chigger in field conditions, the greater will this increase become."

HARRISON, J. L. **The Effect of Grassfires on Populations of Trombiculid Mites.** Reprinted from *Bull. Raffles Museum*. Singapore. 1956, Dec., No. 28, 102-11, 3 figs.

"1. The burning of grass has been suggested as a means of controlling mite typhus (scrub typhus). Continued observations on marked rats in an area of grassland burnt twice during the period provides experimental evidence of the effect of such burning.

"2. Grassland in Malaya is usually of small extent, interspersed with

scrub. Burning during a short dry spell destroys dead leaves of grass and the early regenerating scrub vegetation, but leaves the underground rhizomes of the grass (*Imperata cylindrica*) unharmed. The grass rapidly recovers, so that the net effect is to perpetuate grassland.

"3. In the burnt areas there was an increase in the numbers of *Rattus exulans* trapped, and a decrease in the other species, *R. argentiventer*, *R. jalorensis*, and *R. whiteheadi*. Marked individuals which had disappeared from the area returned later, so that the effect was a temporary change of range rather than any destruction of the rats.

"4. The numbers of *Trombicula akamushi* and *T. deliensis*, the vectors of mite typhus, were estimated from infestation rates. *R. exulans* is a poor host of these mites in Malaya so that comparisons were not wholly satisfactory. The numbers of the more numerous *T. akamushi* dropped sharply after the fire, but did not disappear, and recovered over the next two or three months. The numbers of *T. deliensis* and of *Walchia lewthwaitei* were unchanged.

"5. It is concluded that the burning has little direct effect on the mites, but by temporarily destroying the ground cover produces conditions which are temporarily too dry for them. Against any advantage of burning must be set the resulting perpetuation of grassland which appears to provide conditions particularly favourable to the typhus vector."

CAPUTO, C. Contributo all'epidemiologia delle febbri dermotifosimili.

La febbre bottonosa in Provincia di Savona durante gli anni 1942-1954. [Contribution to the Epidemiology of Typhus-Like Fevers. (Boutonneuse Fever in the Province of Savona from 1942 to 1954)]

Igiene Moderna. 1957, Jan.-Feb., v. 50, Nos. 1/2, 45-56. [16 refs.]

English summary (6 lines).

Boutonneuse fever is stated to be widespread around the Mediterranean littoral but according to the author, who is the Provincial Medical Officer, Savona province is an endemic focus. The affected area runs along the Ligurian coastline for about 40 km. and though agricultural workers are most affected only occasional cases are found in the hinterland. The disease is transmitted usually by the bite of the dog tick *Rhipicephalus sanguineus* but ocular infection is possible and the author reports a case where infection occurred while crushing ticks on a dog [*i.e.*, through intact skin?]. From 1942 to 1954 there have been regular manifestations of the disease in the area during the warm weather, most cases occurring in August. 131 cases were found in the period with a maximum of 21 in 1952. Notification is compulsory but in spite of this the author thinks that the actual numbers are much higher, especially since the introduction of aureomycin and chloramphenicol has made the prognosis good, and the duration of the disease is now only a few days.

The tick is also found in the sand, and in view of the great popularity of the Ligurian beaches this is likely to have an effect on "tourism".

For prevention he suggests an attack on the winter quarters of the tick in cracks in stone and woodwork, repellent chemicals for dogs and other animals, treatment of cattle and dog hides with BHC, and careful supervision of the beaches.

W. K. Dunscombe

LUTYŃSKI, R., RAGINIS, Zofia, ZIEMICHÓD, T. & KOŹMIŃSKA, Alicja. Ognisko gorączki Q w Krakowie. [**Q Fever Outbreak in Krakow**] *Przegląd Epidemiol.* Warsaw. 1957, v. 11, No. 1, 69-79. [15 refs.] English summary.

An account is given of the first outbreak of Q fever recognized in Poland. 2 workers at a zootechnical station in the Krakow area acquired the disease in April 1956 while taking samples of wool from sheep imported from Rumania some months previously. 11 other cases then occurred among workers in the same laboratory; 7 had been in direct contact with the wool, 1 had handled a laboratory notebook used by the first 2 patients, and 3 became infected from contaminated laboratory clothing. The diagnosis was established by serological means and by the isolation of a strain of *R. burneti* from the blood of a patient and from a sample of wool. A brother of 1 of the patients developed the disease, and further cases were discovered retrospectively among farm workers and others who had handled the sheep after arrival from Rumania. 5 cases also occurred at a laundry to which infected clothing was sent.

D. J. Bauer

LESHCHINSKAIIA, E. V., POVALISHINA, T. P. & DZAGUROV, S. G. **The Distribution of Q Fever in the U.S.S.R. (Q Fever in the Chkalov Oblast).** *Problems of Virology.* London. 1957, v. 2, No. 1, 8-11. [11 refs.] [Translated from Russian.]

FISER, P. **Phase Variation of *Rickettsia (Coxiella) burneti*. Study of the Antibody Response in Guinea Pigs and Rabbits.** *Canadian J. Microbiol.* Ottawa. 1957, Apr., v. 3, No. 3, 435-45, 4 figs. [16 refs.]

Complement-fixation tests on the sera of guineapigs or rabbits infected or vaccinated with *Rickettsia burneti* (Nine Mile and Christie strains) showed that antibodies reacting with antigens prepared from *R. burneti* strains which had not been fully egg-adapted (Phase 1 variants) generally failed to become detectable for at least 20 days, while antibodies reacting with antigens from fully egg-adapted strains (Phase 2 variants) were detectable soon after inoculation. The antigen in Phase 1 variants which determines the production of the late-appearing antibody seemed to be masked by the antigen responsible for the formation of the antibody which develops soon after infection or vaccination. This masking antigen

appears to behave as a surface antigen. The results also indicated that the Nine Mile strain lost the surface component of Phase 1 on changing to Phase 2 in the course of egg adaptation, together with components responsible for cross reactions with the Christie strain.

This work may explain anomalous findings obtained in serological tests on different strains of *R. burneti*, as the results of complement-fixation tests would be affected by the particular phase in which the strain used as an antigen happened to be.

R. S. F. Hennessey

BARTONELLOSIS

PEREZ ALVA, S. La maladie de Carrion. Essai d'infection expérimentale de la souris blanche par voie intranasale par *Bartonella bacilliformis*. [Attempt to Infect White Mice intranasally with *Bartonella bacilliformis*] *Bull. Soc. Path. Exot.* 1957, Mar.-Apr., v. 50, No. 2, 184-8. [31 refs.]

The following is a translation of the author's summary:—

216 white mice were inoculated intranasally with different strains of *Bartonella bacilliformis*. Cultures were made on Noguchi's medium, blood agar and Hercelles-Torrevalva-Aldana medium, modified by Gidman, at 28° C. for 3 to 5 days.

Substances inhibiting resistance were used, namely, cortisone, *Salm. enteritidis* toxin, mucin, hyaluronidase and Largactil [chlorpromazine]. Blood cultures and staining (Giemsa and Macchiavello) of the blood and organs of the mice were carried out. In no case could infection of this animal be produced.

H. J. O'D. Burke-Gaffney

YELLOW FEVER

In this section abstracts are arranged as far as possible in the following order:—epidemiology, aetiology, transmission, pathology, diagnosis, clinical findings, treatment, control.

BOSHELL M., J. Marche de la fièvre jaune selvatique vers les régions du nord-ouest de l'Amérique centrale. [The Progress of Jungle Yellow Fever towards the North-West of Central America] *Bull. World Health Organization.* Geneva. 1957, v. 16, No. 2, 431-6.

The epizootic of yellow fever which started in Panama in 1950 spread rapidly through that country, Costa Rica and Nicaragua, and came to an

apparent end half-way through Honduras in 1954, since when it has shown no signs of recrudescence. There is now a period of suspense in which the possibility of further extension to the north must be urgently considered. Review of the epidemiology reveals, however, unknown or imponderable factors as well as those which are understood.

Haemagogus spegazzinii falco may well have been the vector through most of the epizootic, but cannot be found in some places to which it extended. Several other *Haemagogus* mosquitoes must be considered, and present research on *Haemagogus equinus* may prove revealing. There are three genera of monkeys concerned: *Cebus*, *Ateles* and *Alouatta*, the first of which survives infection while the second two are virtually exterminated by the epizootic. *Cebus* may have been the most important reservoir; it persists almost alone in the area the epidemic has covered and somewhat to its north, but comes to an end on the borders between Honduras and Guatemala.

Other factors bearing on the spread of the epizootic are the nature of the forest and the extent to which it is broken up, the temperature—low values of which may delay rather than stop an epizootic—and the humidity. Inexplicable happenings such as the recrudescence of the disease in Nicaragua after six months' quiescence in 1953 must also be taken into account and the epidemiologist must bear in mind what could conceivably happen and not only what is probable.

It is impossible to forecast optimistically that the epidemic is at an end and will not spread northwards. All territories which have at any time in the past been invaded by yellow fever must be considered at risk, and those in which the disease has been recently prevalent must be considered as sources of danger for several years; a strict surveillance mechanism is needed in Honduras for at least two years. The chief risk is that the disease should extend to towns where it might be transmitted by *Aedes aegypti*. Past experience shows that *Aedes* control is of only partial value, whereas *Aedes* eradication is possible and can be permanent in its effects. The author therefore advocates this practice in all places which might possibly be at risk of invasion.

[See also ELTON, this *Bulletin*, 1955, v. 52, 1075.] G. Macdonald

PANTHIER, R. & HUSSON, R. A. Vaccination antiamarile (17 D) et allergie.

[**Yellow Fever Vaccination (17 D) and Allergy**] *Bull. Soc. Path.*

Exot. 1957, Jan.-Feb., v. 50, No. 1, 23-8.

Since 1953 it has been the rule at the Pasteur Institute, Paris, to enquire of all persons attending there for yellow fever vaccination whether they have previously suffered from allergic disease and, if so, to carry out on avowed allergic subjects a preliminary intradermal test with 0.1 ml. of 17D vaccine. In cases where the cutaneous reaction is very strongly positive, further immunization is deferred for at least one month, when

complementary scarification with Dakar vaccine is practised without fear of allergic sequelae. When the cutaneous reaction is mild, 0.4 ml. of 17D vaccine is administered subcutaneously, and only very exceptionally does any general allergic reaction follow. When the reaction to the test is negative, the ordinary dose (0.5 ml.) of 17D vaccine is given subcutaneously, and to date no general allergic reaction has followed. Among persons vaccinated subcutaneously, without the preliminary intradermal test, however, a number of cases of urticaria and, more rarely, of adenopathy have been observed, mostly among young (2-3-year-old) children and less frequently in adults of 35 to 40 years of age.

Secondary reactions following a single intradermal inoculation of 17D vaccine are of two types: those due to the action of the immunizing virus (about 4%); and those of an allergic nature, *e.g.*, urticaria, eczema, asthma, Quincke's oedema, appearing 2 to 9 days after the injection and varying in intensity.

In accordance with the procedure indicated above, 50,000 persons have been vaccinated at the Institute since 1953, and of that number 18,000 remained under close observation. Of the latter number 690 (3.8%), with a history of allergy, were intradermally tested and in the case of 85 (0.47% of the total vaccinated or 12.3% of the 690 allergic subjects) the cutaneous reaction was strongly positive and entailed deferment of further immunization. Among the 85 strongly positive reactors 4 (4.7%) developed general systemic reactions and 4 (4.7%) general allergic reactions (urticaria, asthma, etc.), while among 605 allergic subjects, whose intradermal test had been weakly positive, 2 (0.33%) experienced general allergic reactions. Of the remaining 17,300 persons vaccinated one developed severe urticaria, one mastitis, and 5 (4 axillary) adenopathies.

As regards the immunity conferred on those allergic subjects who had received only one intradermal injection: one month after the injection the serum was shown, by Theiler's intracerebral protection test, to contain sufficient antibody to increase the average survival time in mice by at least 48 hours and to have an antibody titre of between 10 and 100 PD50. After complementary immunization effected by Dakar vaccine the titre of the serum was found to be between 100 and 1,000 PD50. From these results it follows that the presence of serum antibody resulting from the intradermal injection of 17D in no way prevented the later administration of Dakar vaccine from raising the antibody titre to a level ordinarily demonstrable after the subcutaneous inoculation of 17D. It is, therefore, advocated that when primary vaccination has to be limited to an intradermal injection of 0.1 ml. of 17D vaccine, immunization should be completed 1½-2 months later by scarification with Dakar vaccine.

[In 1953 KOUWENAAR (this *Bulletin*, 1953, v. 50, 928) expressed the view that the risk of allergic reaction following yellow fever vaccination will be obviated only when the scarification technique is substituted for subcutaneous injection. With respect to antibody content in the sera of persons vaccinated against yellow fever, it may be stated that a titre of

about 500 PD₅₀ is ordinarily obtained after a single vaccination with 0.5 ml. of 17D vaccine administered subcutaneously.] G. Stuart

BOIRON, H. De l'influence des revaccinations anti-mariques sur le taux de l'immunité humorale. [The Influence of Revaccination against Yellow Fever on the Degree of Humoral Immunity] *C.R. Soc. Biol.* 1956, v. 150, No. 12, 2219-21.

Although the presence of serum antibody in human beings who have been vaccinated against yellow fever is only indirect evidence of immunity to that disease, it is still the only available experimental evaluation that can be carried out in man. Moreover, experience has shown that persons possessing a high antibody content in their blood are in fact refractory to yellow fever.

The present paper gives the results of an investigation devised to ascertain whether, in persons previously vaccinated, revaccination is efficacious only if the serum contains little or no specific antibody, or whether, in the case of persons whose sera still contain appreciable amounts of such antibody, revaccination reinforces the immunity already established.

As regards the first part of the question: revaccination was performed on 2 volunteers whose sera, on mouse-protection testing intracerebrally, had proved capable of neutralizing less than 10 mouse LD₅₀ of virus; retesting 45 days after revaccination showed that both sera completely protected mice against the inoculation of more than 1,000 mouse LD₅₀.

In an attempt to answer the second part of the question the author carried out a series of sero-protection tests on blood samples taken from 2 other volunteers before and 25 days after revaccination. In these tests serial 2-fold dilutions of each serum up to 1 in 128 were mixed with a suspension of virus so as to ensure that each mouse received intracerebrally 10 LD₅₀ of neurotropic yellow fever virus. In a dilution of 1 in 128 the serum of the first of these volunteers completely neutralized 10 LD₅₀ both before and after revaccination. In the second volunteer, however, the highest dilution of pre-revaccination serum capable of neutralizing 10 LD₅₀ of the virus proved to be 1 in 8, whereas the post-revaccination serum in a dilution of 1 in 128 completely protected mice against the same quantity of virus. The presence of appreciable quantities of antibody in the serum before revaccination would not appear, therefore, to impede the production of new antibodies. In the author's view, yellow fever virus, when inoculated into an immune person, is rapidly neutralized, but, however brief its passage, it is still capable of stimulating the defence mechanism of the body and elevating the antibody titre of the serum.

G. Stuart

DENGUE AND ALLIED FEVERS

ROWAN, L. C. & O'CONNOR, J. L. **Relationship between some Coastal Fauna and Arthropod-Borne Fevers of North Queensland.** [Correspondence.] *Nature*. 1957, Apr. 13, v. 179, 786-7.

In mouse-protection tests with 50 LD₅₀ of the Hawaiian strain of dengue I virus carried out with sera from 38 birds caught along the North Queensland coast evidence of the presence of antibody was found in 4 of 14 red-necked stints (*Calidris ruficollis minuta*), 1 of 3 sharp-tailed sandpipers (*C. acuminata*), 1 grey-tailed tattler (*Heteroscelus brevipes*) and a silver gull (*Larus novaehollandiae*). In similar tests with sera from 28 flying foxes (*Pteropus scapulatus* and *Pt. gouldi*) 3 sera gave protection against dengue I virus, 1 against dengue II (New Guinea strain), 4 against Murray Valley encephalitis, 1 against Japanese B encephalitis and 1 against West Nile virus.

D. J. Bauer

RABIES

WELLS, K. F. **The Rabies Menace in Canada.** *Canadian J. Pub. Health*. 1957, June, v. 48, No. 6, 239-43.

Until 1947, when in the Northwest Territories a disease known to the Eskimos for 50 or 60 years as wild fox disease was definitely diagnosed as rabies, all outbreaks of animal rabies in Canada had occurred in the older thickly populated areas bordering on the United States, and infection was confined to domesticated animals, particularly the dog. In these outbreaks the source of infection had been dogs entering the country from the United States or imported from other infected countries. Since 1947, however, the presence of rabies having been established in the eastern, central and western areas of the Northwest Territories and its existence confirmed in the fox and wolf, the source of infection in Canada has changed from the dog to wild animals, especially the fox.

In 1947 diagnosis of wildlife rabies was first established at Baker Lake, 2,000 miles north of Winnipeg, Manitoba, in the Northwest Territories. As a result of mass vaccination of work dogs in the affected area, the disease appeared to subside and thereafter it presented no threat to the southern parts of the country until June 1952, when an outbreak, originating from the Northwest Territories, was reported in northern Alberta. This outbreak, which spread through the province of Alberta and the northern areas of British Columbia, Saskatchewan and Manitoba, has now been brought under control, but the threat still exists in northern Alberta and British Columbia. Another outbreak, this time in Ontario in 1955-56, followed the diagnosis of rabies in a fox at Iroquois Falls

during the late autumn of 1954. This outbreak, originating in the north and extending southwards, ultimately involved a number of counties in southern Ontario and provided the following incidence: between 1 April 1955 and 31 March 1956: 137 positive cases, of which 23 (16·8%) were in dogs and 89 (64·9%) in wild animals (85 or 62% in foxes); in 1956 between 1 April and 31 August: 61 positive cases, of which 2 (3·2%) were in dogs and 52 (85·2%) in wild animals (51 or 83·6% in foxes). That the disease has its reservoir in wildlife is, therefore, abundantly clear.

Control measures present, in these circumstances, a very real problem. Their purpose is not to eliminate wildlife predators but to reduce their numbers below the threshold level for disease spread and to prevent by trap lines as many as possible of these predators from filtering into fringe farming or urban areas, thereby protecting both human and livestock life. In addition to reducing the wildlife population, measures include controlling the movement of dogs and the vaccination (with high egg-passage chicken embryo vaccine) of all dogs and cats in the settled areas. Vaccination is regarded as an adjunct to, and not as a substitute for, absolute dog control.

[A comprehensive account of the wildlife reservoirs of rabies in Canada was given by PLUMMER in 1954 (this *Bulletin*, 1954, v. 51, 1239). Means to determine the contact and density threshold required to support a rabies epizootic among wild animal vectors are now under consideration.]

G. Stuart

MÁLAGA ALBA, A. & CAMPILLO SAINZ, C. Rabia humana transmitida por murciélagos, confirmación del primer caso en México. [**Human Rabies transmitted by Bats. Confirmation of the First Case in Mexico**] *Bol. Oficina Sanitaria Panamericana*. 1957, June, v. 42, No. 6, 567-70. [15 refs.]

The authors, from Mexico, refer to the literature on bat rabies and then give a detailed description of a case in a girl of 17 in Taxco, Mexico, who was bitten on the left thumb by a bat in September 1955, and who developed rabies 24 days later and died within a week. The diagnosis was confirmed by the finding of Negri bodies, the inoculation of mice and neutralization tests. This is the first human case of rabies transmitted by a bat to be confirmed by laboratory methods in Mexico.

H. J. O'D. Burke-Gaffney

IRONS, J. V., EADS, R. B., GRIMES, J. E. & CONKLIN, Alice. **The Public Health Importance of Bats.** *Texas Reports on Biol. & Med.* 1957, v. 15, No. 2, 292-8, 1 fig.

Since the first case of rabies in an insectivorous bat was reported from Florida in June 1953 by VENTERS *et al.* [this *Bulletin*, 1954, v. 51, 686],

rabies virus has been isolated on numerous occasions from different species of insectivorous Chiroptera in the United States, particularly in the south-western states, where the greatest number of isolations have been made from the Mexican free-tailed bat *Tadarida mexicana*. The question of the epidemiological and epizootiological significance of these findings has, therefore, been raised, because of the possible role of these insectivorous flying mammals in the natural transmission of infection to foxes, skunks, raccoons and other wild carnivores, to domestic animals such as livestock, dogs and cats, and directly to human beings.

In Texas, where rabies in domesticated animals constitutes a serious problem and where the high level of infection in dogs and wildlife is reflected in the 35 human deaths reported in the last 12 years (5 deaths in 1956 alone), there have been 22 cases of bat bites in human beings during the period 1954-56. Involved in these episodes were 9 free-tailed bats (*T. mexicana*), 5 red bats (*Lasiurus borealis*) and 1 hoary bat (*Lasiurus cinereus*); 2 of the *T. mexicana* and 3 of the *L. borealis* were proved to have been rabid at the time of biting. The 8 persons bitten by these rabid bats experienced no untoward effects either from the bites or the subsequent anti-rabies treatment. All the bites in this series resulted from the bats being handled, none from an unprovoked attack.

Of the two species from which virus was isolated the free-tailed bats are colonial and abundant over much of Texas during the warmer months of the year in caves and in and around human habitations. In the vicinity of caves occupied by these bats in summer large numbers of raccoons, skunks and foxes congregate and evidence exists that during this period bats form important dietary items for these animals. That the opportunity exists for such bats to transmit the disease to wild animals is, therefore, clear. Moreover the close colonial association of this species of bat with human dwellings represents a potentially dangerous situation for man and his domestic animals. The red bat *L. borealis*—a solitary, tree-dwelling species common throughout Texas in the summer months—comes to human attention mainly because of the fact that the female, which carries her young until able to fend for themselves, often is overcome by their weight and falls to the ground, where she may be picked up by children and household pets. Rabies virus was isolated from 5 of the 95 red bats collected in Texas between 1954 and 1956.

That insectivorous bats may be of public health significance is suggested by the occurrence of 2 human rabies deaths in Texas—one in 1951 and the other in 1956—believed to have resulted from exposure to such bats. From available evidence, however, the authors are of opinion that, while insectivorous bats definitely represent a public health problem, “the extent of their involvement in the basic infection chain of rabies in nature remains to be clarified”.

[According to the Expert Committee on Rabies in its third report (*ibid.*, 1957, v. 54, 809), there is no direct evidence of natural transmission of rabies from insectivorous bats to man or lower animals. Despite this,

the public health significance of rabies in such bats cannot be overlooked, since there have been at least 15 instances in which proven rabid bats have bitten human beings. Approximately half of these attacks were unprovoked. Circumstantial evidence has incriminated insectivorous bats as the source of infection in 2 human rabies deaths (*vide supra*).]

G. Stuart

BELL, J. F., BURGDORFER, W. & MOORE, G. J. **The Behavior of Rabies Virus in Ticks.** *J. Infect. Dis.* 1957, May-June, v. 100, No. 3, 278-83. [15 refs.]

The possible role of haematophagous arthropods in the epizootiology of rabies seemed to the authors to warrant more extensive investigation than that already carried out. The likelihood of arthropods becoming infected obviously depends upon the presence of virus in the peripheral blood of the rabid host animal, but in this connexion differences of opinion exist as to whether viraemia does in fact occur in animals infected with rabies virus. In order to obtain further clarification on this point, therefore, and to acquire further data on the infection of ectoparasites with rabies virus, the authors conducted a series of experiments with ixodid and argasid ticks; the results are given in the present article.

In the experimental work use was made of: rabbits and guineapigs as hosts for ticks, and Swiss mice for titrations; the ixodid ticks *Rhipicephalus sanguineus* and *Dermacentor andersoni* and the argasid ticks *Ornithodoros moubata*, *O. turicata* and *O. parkeri*; and 2 strains of rabies virus—a Pasteur strain and one isolated from a bat.

In the first set of experiments results showed that in rabbits infected with fixed rabies virus, viraemia could not be detected, even when techniques supposed to evoke its occurrence were employed. Further, the ixodid ticks *R. sanguineus* and *D. andersoni*, which engorged upon such rabbits, did not become infected.

Because of repeated failures to demonstrate virus in the blood of infected rabbits or in the ticks fed upon infected rabbits, the authors abandoned further efforts to infect ticks naturally and resorted, in a second set of experiments, to artificial infection by means of the glass capillary tube and membrane feeding techniques. Results showed that in ticks infected by such means, virus survived in ixodid ticks (*D. andersoni*) for only 3 days, in nymphal argasid ticks (*O. moubata* and *O. turicata*) for approximately 14 days, and in adult argasid ticks of these 2 species for 20 days. Further, no evidence of multiplication of rabies virus could be obtained either in ticks (*D. andersoni*, *O. moubata* and *O. turicata*) fed upon infectious material or in ticks (*O. moubata* and *O. parkeri*), which were directly inoculated with virus suspensions. These findings suggest that rabies virus neither persists for a long period nor multiplies in ixodid or argasid ticks.

Finally, transmission experiments with infected ticks were performed. In one experiment second nymphal stage *O. moubata* and *O. turicata*

were engorged partially through mouse skin membranes upon a suspension of virus (bat strain) in blood—the titre of the supernate being log 4.6/0.03 ml.; the ticks completed their feeding on newly weaned mice, which were then kept under observation for 3 months; no evidence of rabies was noted. In another experiment adult *D. andersoni* ingested 0.01 to 0.03 ml. of a virus suspension prepared from brain tissues of infected mice; thereafter the ticks completed their feeding on newly weaned guineapigs; no transmission of virus occurred, all animals remaining well during the 3-month observation period.

In view of the findings indicated above, the authors believe that ticks are of no significance in the epizootiology of rabies. *G. Stuart*

AKSEL, I. S. & AYKAN, T. B. Le comportement en culture du tissu cérébral infecté par le virus rabique. L'évolution des corpuscules de Negri *in vitro* dans le tissu cérébral rabique. [**Behaviour of Cerebral Tissue Cultures infected with Rabies Virus. *In vitro* Evolution of Negri Bodies in Rabies Cerebral Tissue**] *Ann. Inst. Pasteur.* 1957, July, v. 93, No. 1, 30–35, 3 figs.

The English summary appended to the paper is as follows:—

“The authors attempted to culture rabies infected cerebral tissue by introducing fragments of such tissue into a medium constituted of a liquid phase (equal parts of horse serum and Tyrode solution) and a solid phase (coagulated chicken plasma).

“It was not possible to obtain a culture of cerebral tissue because of the typical coagulation necrosis which always occurs.

“However the virus remained viable during a month, which agrees with the results obtained by other workers.

“The authors also demonstrate that Negri bodies also preserve their integrity during a month; it seems therefore that Negri bodies are independent of the cellular components.

“The emulsion of the 30 days old cultures were inoculated into rabbits, and induced paralysis and the formation of Negri bodies.”

HABEL, K. **Rabies Prophylaxis in Man.** *Pediatrics.* Springfield, Ill. 1957, May, v. 19, No. 5, 923–36. [48 refs.]

The material covered by this review will be familiar to readers of this *Bulletin*, but its great value lies in the fact that it has been written by an outstanding expert who not only brings together the relevant literature but lends to the review the authoritative stamp of his own wide knowledge and experience.

Dr. Habel begins with a general reference to the incidence of rabies in the United States and points out that it has now been shown that in that country there are reservoirs other than the dog, for example, foxes, skunks and bats. He then discusses the pathogenesis of rabies, its

incubation period, the handling of biting animals and the local treatment of wounds. Vaccination is discussed under the headings of types of vaccine, potency, dosage, complications and efficacy. On this last controversial point the author gives a clear personal opinion. He considers that most mild exposures to rabies would not result in the disease, even without specific prophylaxis, while many severe exposures, especially with short incubation periods, will result in a fatal infection, no matter how much vaccine is given. "However, there is a large group of individuals receiving moderate exposure for whom the prompt use of vaccine will spell the difference between survival and death from rabies after a prolonged incubation period."

The experimental basis, field trials and present status of immune serum are next discussed, after which the author sets out recommendations for specific prophylaxis. These are considered under the headings of the animal responsible, nature of exposure, age of patient, time relationships, re-exposure, and immunization against anticipated exposure.

Dr. Habel ends his review by touching briefly on problems for future research which are aimed first "at reducing or eliminating the dangers due to the prophylactic measures themselves and improving the efficacy of these measures, and finally searching for more efficient and more practical new methods". This theme is elaborated in terms of rabies vaccines, their nature and preparation, the interrelationships between such vaccines and antiserum, and the need to include rabies in any programme of chemotherapeutic research directed at finding antiviral agents.

Those who require a clear and up-to-date appraisal of the present position regarding rabies prophylaxis, presented with an admirable economy of words, could not do better than read this excellent review.

H. J. O'D. Burke-Gaffney

YAOI, H., GOTO, N., YAMASAWA, R. & NAGATA, A. **Studies on the Rabies Vaccine. XIVth Report: On the Effects of PVL and Cortisone upon Immunizing Power of Anti-Rabies Vaccine.** *Yokohama Med. Bull.* 1956, Dec., v. 7, No. 6, 371-82, 1 fig. [40 refs.]

That the rate of antibody production consequent on anti-typhoid vaccination could be greatly accelerated by the simultaneous injection of purified vaccine lymph (PVL) was first proved experimentally in 1939 by YAOI (*Japan. J. Exp. Med.*, 1939, v. 17, 295). Since then Yaoi and his collaborators have observed in man and in experimental animals alike a similarly rapid rise in antibody titre when other bacterial vaccines were used in combination with purified vaccinia virus. In order to determine whether in anti-rabies vaccination the simultaneous administration of PVL would be followed by a like result and whether, in such combined treatment, the substitution of cortisone for PVL would have any comparable effect, the authors conducted a number of protection tests on mice and of serum-virus neutralization tests on rabbits, following the

administration, to groups of these animals, of anti-rabies vaccine alone or in combination with either PVL or cortisone acetate.

For immunization 2 lots of vaccine differing in antigenic potency were used: for rabbits a 10% emulsion of guineapig brain infected with the Nishigahara strain of fixed rabies virus was employed, after inactivation by the combined action of 0.1% Merzonin and heat at 37°C. for 5 days; for mice the same emulsion, similarly inactivated for 8 days and thereafter kept at room temperature for 3 months prior to use, was diluted to 0.5%, in order to meet the requirements of the protection experiments.

In the first mouse protection experiment comprising 5 groups of white mice weighing 10–12 gm., each animal in 4 groups received intraperitoneally 0.25 ml. doses of vaccine: in groups I and II on 3 and on 6 alternate days, respectively; in group III on 3 alternate days, on each of which 0.1 ml. of PVL was also injected under the skin of the thigh; and in group IV on 3 alternate days, on each of which 1 mgm. of cortisone acetate was also injected into the thigh muscles. Group V served as control. In the 3-dose groups and in the 6-dose group intracerebral challenge was made 7 days and 14 days, respectively, after the start of immunization. Results showed the MLD protective values in groups I, II, III and IV to be, respectively, 5,000, 16,000, 50,000 and 500. In the second mouse protection experiment also comprising 5 groups of mice; group I received vaccine and PVL simultaneously on 3 alternate days; group II vaccine alone on 6 alternate days; group III vaccine on 3 alternate days and cortisone intramuscularly on each of the last 3 days before challenge; and group IV cortisone alone, time and mode of administration as in group III. Group V served as control. All groups were challenged 14 days after the beginning of treatment. Results showed the MLD protective value in groups I, II, III and IV to be, respectively, 1,300, 160, 25 and –16. Thus the group receiving 3 simultaneous injections of vaccine and PVL showed a protection index 8 times greater than that of the group receiving 6 doses of vaccine alone, and 50 times greater than that of the group receiving vaccine and cortisone. Whereas, then, combined vaccination with PVL produced an immunity several times greater than that obtainable from twice the amount of vaccine alone, the simultaneous use of vaccine and cortisone resulted in a very marked reduction in the immunity conferred. From the results of this experiment it also emerged that the mice receiving cortisone alone showed a marked increase of susceptibility to the virus.

Neutralization tests on the sera of rabbits treated with vaccine alone and in combination with either PVL or cortisone were then performed. Rabbits weighing 2,500–2,900 gm. were placed in 3 groups and injected intradermally, each with 0.2 ml. of vaccine daily, on 7 successive days. Group I received vaccine alone; group II 7 doses of vaccine and 2 of PVL (0.2 ml. and 0.3 ml. subcutaneously on the 1st and 4th day of immunization, respectively); and group III 7 doses of vaccine and, in addition, daily intramuscular injections of cortisone in a dosage of 4

mgm./kgm. of body weight for 20 days. The animals were bled 10, 14 and 21 days after the start of immunization; their sera were separated by centrifugation and inactivated at 56° for 30 minutes in the water-bath. Results showed the mean neutralization index (NI) at 10, 14 and 21 days to be, respectively, 116, 853 and 2,050 in group I; 483, 1,310 and 4,166 in group II; and 46, 133 and 766 in group III. Vaccine combined with PVL gave rise, therefore, to a rapid and abundant formation of antibodies in rabbits (*e.g.*, 4 times greater at the 10th day than that evoked on that day by vaccine alone), while vaccine combined with cortisone resulted in a marked inhibition of antibody formation.

G. Stuart

MAGGI, Nicola. Contributo allo studio degli accidenti sincopali da trattamento antirabbico. [**Syncopal Accidents in Antirabic Treatment**] *Igiene e San. Pubblica*. Rome. 1957, Mar.-Apr., v. 13, Nos. 3/4, 169-76. English summary.

The author from the provincial laboratory at Bari points out that of the 2 main varieties of "accidents" in antirabic treatment, syncopal conditions are more frequent than the so-called "paralytic" accidents, and that in man only "slight" accidents occur as the result of intravenous injection of rabies vaccine, in contrast to the condition in rabbits or dogs where an acute fatal asphyxia may occur. In these 2 groups of animals the condition may be due to a sufficient dose of thrombokinase getting into the circulation and causing coagulation of the blood in the right heart or pulmonary vessels.

He has therefore carried out experiments on rabbits to ascertain whether the prothrombin time is shortened after intravenous injection of homologous nervous substance, and also to test the tolerance in rabbits previously given heparin, to intravenous injection of doses greater than 1 MLD. The results showed that (i) the prothrombin time was reduced; (ii) this became shorter the closer the inoculating dose came to 1 MLD; (iii) heparin given as 100 mgm. in 2 cc. protected the rabbits against 4 MLD.

As therefore heparin apparently acts as a preventive of the massive coagulation of the circulating blood, the author suggests that if a syncopal accident occurs during antirabic treatment heparin might be used, prudently.

W. K. Dunscombe

MIKHALENOK, Z. V. **A New Preparation: Anti-Rabies Gamma-Globulin.** *Problems of Virology*. London. 1957, v. 2, No. 1, 52-3. [Translated from Russian.]

In the Mechnikov Institute of Vaccines and Sera in Moscow, anti-rabies gamma globulin has been prepared from the serum of horses hyper-immunized with a strain of fixed rabies virus.

Treatment with this preparation combined with vaccination is recommended for the specific prophylaxis of rabies after deep or multiple bites at any site or bites in the face or head by animals known or suspected to be rabid, especially wolves.

Anti-rabies vaccination is not always effective after severe bites near the head when the incubation period is less than 30 days. Treatment with gamma globulin seems to establish passive immunity which develops at once and lasts for 2-3 weeks, by which time active immunity induced by vaccination will have developed.

The gamma globulin is given intramuscularly in a dose of 0.25 ml./kgm., after a preliminary desensitization with 0.1 ml. diluted 1 in 10 with distilled water, given subcutaneously. 30 minutes after the desensitization, the whole dose is given, heated in water warmed to 36-37°C.

The preparation should be given as soon as possible after the bite (within 72 hours) and administration of rabies vaccine (Fermi type) is started 24 hours later in daily doses of 5 ml. for 21 days.

After very severe bites up to 5-7 injections of gamma globulin may be given at intervals during 1 to 2 days: in these cases the interval between the gamma globulin and vaccination should be 2-3 hours.

This preparation is also recommended when rabies vaccine has to be stopped because of paralytic accidents: up to 3-6 daily doses may be given at intervals in 1-2 days, depending on the health of the patient and his tolerance to the gamma globulin. *H. J. O'D. Burke-Gaffney*

CECCALDI, J., LEPISSIER, H. & MERVEILLE, P. Premier cas de rage observé en A.E.F. chez un chien vacciné préventivement. [**First Case of Rabies seen in French Equatorial Africa in a Dog previously vaccinated prophylactically**] *Bull. Soc. Path. Exot.* 1957, Mar.-Apr., v. 50, No. 2, 197-200.

The following is a translation of the authors' summary:—

The authors report the first case of rabies seen at Tchad, French Equatorial Africa in a dog vaccinated prophylactically 7 months and 19 days earlier with 2 injections of Fermi type antirabic vaccine, each of 20 cc., given at an interval of 48 hours.

They stress the need for intensification of prophylactic vaccination of dogs in French Equatorial Africa by means of the schedule set out by LÉPINE, because of an increasingly wide spread of rabies virus in the interior of the Federation. *H. J. O'D. Burke-Gaffney*

PLAGUE

In this section abstracts are arranged as far as possible in the following order:—epidemiology, aetiology, rodent hosts, transmission, pathology, diagnosis, clinical findings, treatment, control.

NGUYEN-VAN-AI. La peste au Sud-Viet-Nam en 1956. [**Plague in South Vietnam in 1956**] *Bull. Soc. Path. Exot.* 1957, Jan.–Feb., v. 50, No. 1, 8–11, 1 fig. [10 refs.]

Plague was known in South Vietnam, Indo-China, in the first decades of this century, but regressed since 1923, with minor foci appearing in 1926, 1934, 1943 and 1948: from 1951–1955, it had apparently disappeared.

In 1956, two old foci flared up and 50 cases were reported. Early in March, plague had been reported in Siemreap, Cambodia; in the beginning of April an epidemic occurred in Tâyninh, South Vietnam, and 35 cases of bubonic plague were found in 2 villages. 4 patients who received no treatment died; the remainder recovered after treatment with streptomycin (2 gm. daily for 1 week, then 1 gm. daily until the temperature fell), with or without other antibiotics and sulphonamides, and with plague antiserum in severe cases.

Early in the outbreak, plague vaccine (EV strain) and antiserum were used prophylactically; this together with treatment of the affected persons had the result that within 1 month no new cases were reported in this region. Early in June, the outbreak had been brought to an end.

Between March and May, pathological material was received from 30 patients already under treatment. 6 blood cultures proved negative, but in 1 of 30 smears from gland punctures, organisms were found morphologically resembling *Pasteurella pestis*. 6 strains were isolated from 14 cultures of pus from buboes. They were of the type usually isolated in Vietnam and were pathogenic for guineapigs and mice.

All strains were sensitive to streptomycin and chloramphenicol and mostly resistant to the other common antibiotics, although there was a variable but limited susceptibility to framycetin, erythromycin, aureomycin, oxytetracycline and neomycin.

4 months later, in mid-August, a second outbreak occurred, this time in Phanhiêt in central Vietnam. There were 15 cases, with 3 deaths all of which occurred in untreated patients. Similar measures to those previously employed brought the outbreak to an end in late September. In 3 of these cases, *P. pestis* was found in pus from buboes.

These two places constitute areas of known endemicity. The author points out that streptomycin is the "heroic" method of treatment of plague—all the 7 patients who died had had none. A few cases resolved with sulphonamides alone. A few days after streptomycin treatment, buboes were found to be negative in direct smears, but in half of them culture was still positive. It is clearly essential that culture should be undertaken where possible before treatment with antibiotics is begun.

H. J. O'D. Burke-Gaffney

SRIKANTAN, T. N., AGARWALA, S. C. & SHRIVASTAVA, D. L. **Studies in the Enzyme Make-Up of *Pasteurella pestis*. Part III. Oxidative Metabolism of Virulent and Avirulent Strains.** *Indian J. Med. Res.* 1957, Apr., v. 45, No. 2, 151-9, 3 graphs. [10 refs.]

"1. The oxygen consumption with 8 virulent and avirulent strains of *P. pestis* using 5 amino acids and 3 sugars did not show any general correlation between virulence and oxidative metabolism.

"2. Older cultures of *P. pestis* showed significantly less oxygen consumption with glucose, ribose and serine.

"3. Chlorotetracyclin, oxytetracyclin and tetracyclin considerably inhibited the oxidative metabolism of *P. pestis*, using glucose and serine. Neomycin, streptomycin and chloromycetin, on the other hand, slightly inhibited the serine metabolism and activated the glucose oxidation. Sulpha drugs tried were without any action."

SAXENA, K. C., SAGAR, P., AGARWALA, S. C. & SHRIVASTAVA, D. L. **Studies in the Enzyme Make-Up of *Pasteurella pestis*. Part IV. Transamination Reactions in Virulent and Avirulent Strains.** *Indian J. Med. Res.* 1957, Apr., v. 45, No. 2, 161-71, 4 graphs. [14 refs.]

"1. Cell-free extract of *P. pestis* catalysed transamination between α -ketoglutaric acid and a number of amino acids to produce glutamic acid.

"2. The optimum pH of the reaction was found to be at 8.0 and even at 8 hours' incubation it did not reach completion.

"3. Extraneous supply of pyridoxal phosphate was necessary only with alanine α -ketoglutarate system.

"4. Among the 14 compounds tested mercuric sulphate showed the maximum inhibition.

"5. Antibiotics and sulpha drugs tried were found to be without any action.

"6. A comparison of transamination reactions between the virulent and the avirulent strains did not show any general correlation between virulence and transamination."

STARK, H. E. **Five New Fleas of the Genus *Thrassis* Jordan, 1929 (Ceratophyllidae: Siphonaptera), a Genus of Known Importance in Plague Transmission.** *J. Parasitology.* 1957, June, v. 43, No. 3, 332-46, 36 figs. on 5 pls. [29 refs.]

ELBEL, R. E. & THAINEUA, M. **A Flea and Rodent Control Program for Plague Prevention in Thailand.** *Amer. J. Trop. Med. & Hyg.* 1957, Mar., v. 6, No. 2, 280-93, 4 figs. [11 refs.]

"Plague appeared in Thailand in 1904 and has been endemic ever since. Two epidemics of plague, one at the end of 1951, and the other early in 1952, prompted the Thai Department of Health to establish

permanent laboratories for plague detection and control in each of the three known plague areas of Thailand. Routine procedures of control and prevention were used.

"The present report discusses the work of these laboratories between February, 1952, and September, 1953, during which period a total of 48,553 domestic rats, *Rattus exulans concolor*, were obtained by live-trapping. These and some animals collected from the fields and forests were tested for the presence of plague which was detected only in *R. exulans* and its flea, *Xenopsylla cheopis*. Indices of this vector were computed monthly and an attempt was made to treat with DDT all villages, cities, or sections of cities, whenever the local *X. cheopis* index rose above 1.0. The major city in each area was studied in detail; wide oscillations were observed in the flea populations which may or may not have been due to the DDT treatment. Notes are given on the other species of rodents associated with *R. exulans*."

HAYASHIDA, T. **Effect of Pituitary Adrenocorticotrophic and Growth Hormones on the Resistance of Rats infected with *Pasteurella pestis*.** *J. Exper. Med.* 1957, July 1, v. 106, No. 1, 127-43, 3 figs. [46 refs.]

CHOLERA

In this section abstracts are arranged as far as possible in the following order:—epidemiology, aetiology, pathology, diagnosis, clinical findings, treatment, control.

POLLITZER, R. **Cholera Studies. 9. Symptomatology, Diagnosis, Prognosis, and Treatment.** *Bull. World Health Organization.* Geneva. 1957, v. 16, No. 2, 295-430. [Numerous refs.]

This detailed study of the clinical aspects of cholera, which consists of approximately 60,000 words and includes nearly 300 references, is a summary of the clinical work on cholera during the last 100 years. There are earlier isolated references, but in nearly every section there is a reference to GRIESINGER's authoritative account of the disease in Virchow's *Handbook* of 1857.

There is a considerable degree of unanimity regarding the incubation period, which is generally placed at about 3 days with occasionally shorter periods down to 24 hours. The clinical types of cholera recognized are usually choleraic diarrhoea, cholerae (an intermediate type), cholera gravis (the classical severe attack), and the fulminant type (*e.g.* cholera sicca).

At the onset the frequency of the occurrence of prodromal diarrhoea is a subject of controversy, but the majority of authors consider it relatively rare. The period of evacuation lasts from a few hours to 5 days or more, but is under 2-4 hours in a relatively few cases, whereas vomiting, on the

contrary, lasts for 24 hours or less in over 60% of cases. Muscular cramps and their cause are discussed. The algid stage is then considered, with its dehydration, circulatory failure, respiratory distress and *vox cholericæ*. The temperature in cholera has brought out considerable divergencies of experience as well as opinion. The author appears to have accepted the decision of the abstracter and some of his contemporaries to question the opinion that cholera is a "disguised febrile disease", but he has not noted some more recent papers which support this idea, one that has always been championed by ROGERS. It is certain that hyperpyrexia was at one time a relatively frequent complication in the stage of reaction, but there are other explanations for this.

A number of very varied complications affecting most of the systems and tissues have been reported by different workers from time to time, but there is little to suggest that any of these could be labelled as true sequelæ since they are so varied and inconstant.

In children and in the aged the disease usually appears to be severe, but in the former the question of diagnosis comes in to complicate the matter.

The inevitable delay in the making of a bacteriological diagnosis makes it necessary to arrive at a *prima-facie* clinical diagnosis, but however skilfully this is done there will never be complete correlation between the clinical and bacteriological diagnosis even in an epidemic, let alone in individual cases. Reference is made to the El Tor vibrio, and to the Celebes clinically classical outbreaks, apparently caused by "choleriform" organisms, but, as the author points out, the importance is epidemiological rather than clinical, since the treatment of the patient is the same whatever the organism isolated.

Prognosis is very variable, but the death rate among the untreated is always high. The figures are widely different in various outbreaks and even at different stages in the same outbreak. There are many factors involved. The previous state of health of the population, previous vaccination, the promptness with which treatment is undertaken are discussed, as also are the various prognostic signs in the earlier stages of the attack.

Treatment falls naturally into three sections, under the headings—specific treatment, infusion treatment, and adjuvant treatment. With ample justification the author labels the first section "Attempts at Specific Therapy" and concludes by expressing the belief that no so-called specific treatment has any serious effect on the course of the disease. However, he reviews at considerable length the various attempts that have been made under a series of headings, including serotherapy, essential oils, kaolin, potassium permanganate, bacteriophage, sulphonamides, and antibiotics. A reference is made to the early history of transfusion treatment; although HERMANN gave water intravenously in a cholera outbreak in Moscow in 1830, it was LATTA (1831) who first used intravenous saline in cholera. It was not very popular until nearly 80 years

later when ROGERS re-introduced it and then suggested the hypertonic saline with which he was much more successful. The author devotes about 20 pages to a discussion of the fluids used, their composition, their preparation, the temperature at which they should be given, the technique of their administration, amount to be given, etc. The pros and cons of plasma administration are discussed and a general opinion that the case for plasma is not yet proven is expressed. The author makes it perfectly clear that some form of infusion treatment is essential and this section constitutes a useful study of the important details often neglected in describing cholera treatment. Under adjuvant treatment, atropine, adrenaline, suprarenal cortical extract, pituitary extract, and cardiac stimulants are mentioned, and finally the treatments of uraemia, hyperemesis and muscular cramps, and diet and general management are reviewed.

L. E. Napier

BANERJEE, S., BHADURI, J. N. & SARKAR, A. K. **Studies on Glucose Tolerance Test in Cholera.** *Indian J. Med. Res.* 1957, Jan., v. 45, No. 1, 9-14.

It is known that patients suffering from cholera may have a high blood sugar but that in some patients the value is low [this *Bulletin*, 1941, v. 38, 583 *bis*]. In amplification of these earlier observations the authors estimated the blood sugar in patients suffering from cholera before and at half-hour intervals on 4 occasions after the intravenous injection of 50 ml. of 25% solution of glucose. The fasting blood sugar levels in the 22 patients studied ranged from 85 to 203 mgm. per 100 ml. blood. In 15 the value was 119 mgm.% or more and in the remaining 7 it was 107 mgm.% or less. Dehydration was present in all cases but was considered to be insufficient to account for the raised blood sugar values.

Half an hour after the intravenous injection of glucose the blood sugar values had increased but in most of the patients the value 2 hours later was lower than that which it had been initially. This, it is suggested, indicates that patients with cholera can utilize satisfactorily injected glucose.

Hyperglycaemia where present, might, it is considered, be caused by glycogenolysis in the liver resulting from excessive secretion of adrenaline. The intravenous injection of glucose might prevent this or stimulate glycogenesis in the liver. The inorganic phosphorus levels in the fasting blood samples were higher than normal. This, it is suggested, might result from conversion in the liver of glycogen to glucose-6-phosphate as an intermediate product in the breakdown of glycogen into glucose and phosphoric acid. [In a condition such as cholera in which there is such gross disturbance of a wide variety of body processes the interpretations which can be placed on these observations are clearly highly speculative.]

A. W. Woodruff

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

In this section abstracts are arranged as far as possible in the following order:—epidemiology, aetiology, pathology, diagnosis, clinical findings, treatment, control.

DONCKASTER, R., SAPUNAR, J. & DONOSO, A. Ensayo terapéutico de la amibiasis intestinal crónica con tetraciclina y cloroquina glicolil-arsanilato de bismuto y control parasitológico con los métodos de Telemann y alcohol polivinílico combinados. [**Therapeutic Trials in Chronic Intestinal Amoebic Patients controlled by the Combined Methods of Telemann and PYA Fixation, with Tetracycline, Chloroquine and Bismuth Glycolyl Arsanilate**] *Bol. Chileno de Parasit.* 1957, Apr.–June, v. 12, No. 2, 24–9. [13 refs.]

The English summary appended to the paper is as follows:—

“ 1.—76 and 61 human cases of chronic amoebic infection were treated with Tetracycline and chloroquine-Bismuth Glycolyl Arsanilate, respectively. Stool and clinical controls were done periodically up to 6 months after treatment.

“ 2.—Stool examinations, one every other day until six were completed, were done according to Telemann's procedure and also with P.V.A. [polyvinyl alcohol] -fixative.

“ 3.—77% of the cases treated with Tetracycline were negative 10 days after treatment, while 60% remained negative after six months. Insofar as chloroquine-Bismuth Glycolyl Arsanilate is concerned, 78 and 42% were negative at the same periods, respectively.

“ 4.—Tetracycline was tolerated best.

“ 5.—Stool preservation with P.V.A.-fixative was shown to be an important parasitological diagnostic tool, specially when simultaneously employed with Telemann's procedure.”

[The doses used for adults were:—

Tetracycline 1.5 gm. daily, in divided doses, for 10 days.

Chloroquine-bismuth glycolyl arsanilate (Neo-Viasept, Hoechst) (containing 75 mgm. chloroquine and 250 mgm. bismuth glycolyl arsanilate in each tablet) 6 tablets daily, in divided doses, for 10 days.]

RELAPSING FEVER AND OTHER SPIROCHAETOSIS

MACARTHUR, W. **Historical Notes on some Epidemic Diseases associated with Jaundice.** *Brit. Med. Bull.* 1957, May, v. 13, No. 2, 146–9.

Apart from tropical yellow fever, the diseases which in epidemic form show jaundice are leptospirosis icterohaemorrhagica, infectious hepatitis

each of these drugs are dissolved in 500 ml. of 5% glucose or normal saline and injected intravenously at the rate of about 40 drops a minute, or slower if there is a rise in temperature or a fall in blood pressure.

The results were: disappearance of pain in 100% of cases within some 24 hours; reduction of temperature to about normal in 80% within 6 hours, erythema and nodules diminishing from the 3rd day and disappearing by the 12th day in 80% of cases. There were about 47% of relapses within 12 months, most of these being in the first 3 months, but they all responded to another dose of the previous treatment.

In subacute reaction while the specific antileprotic treatment is continued, Amplictil may be given in 25 mgm. tablets by mouth, beginning with 1 tablet and rising to 4 on the 4th day. The dosage gradually diminishes from the 7th day to 1 tablet on the 10th day which continues to the 30th day. This treatment gave excellent results in 50% of patients, good in 17.7% and medium in 17.7%. Daily doses of 25 mgm. appeared to prevent or diminish reaction in patients under anti-leprosy treatment.

Side effects of this treatment are low blood pressure, drowsiness and desquamation, but none of these are counted serious. *Ernest Muir*

SMAKA, R. S. & CAPP, A. B. Nova terapêutica da neuralgia leprótica. [A New Therapy of Nerve Pains in Leprosy] *Rev. Paulista Med.* S. Paulo. 1956, July, v. 49, No. 1, 44-53.

The authors, after mentioning various general medicines and local applications for neuritis in leprosy, give their results of its treatment with chlorpromazine (Thorazine or Amplictil). The drug was given intravenously in 80 lepromatous cases with neuritis accompanying erythema nodosum; intramuscularly in 40 lepromatous, 10 tuberculoid, and 10 indeterminate cases; and orally in 40 lepromatous, 7 tuberculoid, and 5 indeterminate.

The intravenous injections were reserved for acute cases where acute reaction accompanied the neuritis, and Amplictil (50 mgm.) was combined with Phenegan [promethazine] (50 mgm.) in 500 ml. of 5% glucose.

The intramuscular injections were given three times at intervals of 2 or 3 days, 25 mgm. of Amplictil being mixed with 50 mgm. of Phenegan and injected at night because of the soporific effect of the latter.

The oral method in the daily schedule described [above] has distinct advantages over the other 2 routes, administration being much easier and the results practically the same.

There was complete relief in 90% of those treated by the intravenous and intramuscular routes, and in 82.7% of those treated by the oral route. The specific treatment may be continued while Amplictil is being given orally. *Ernest Muir*

Leprosy is supposed to have problems different from those of other diseases and offers opportunities to the modern sorcerer, so that not a few select their facts about the disease to suit their ideas, ignoring those that do not agree. Examples are given of leprophobia in a physician who took excessive care in his contact with patients, and of another who was a negative leprophobe and was unnecessarily careless about his contact with infection. Leprophobia "does not exist except as occasion for it may arise. But the background for it, the biblical references, the use or understanding of 'leprous' to mean generally odious or loathsome rather than to refer to a specific process, is probably in some degree present with most people". While there is a strong social-political movement which decries the physician who does not hold with the socialistic trend in leprosy, it is suggested "that the major strengths of the socialistic forces in leprosy derive directly from medical contributions. . . ."

Ernest Muir

BICA, A. N., ROMÁN, J. & SÁENZ, A. C. El problema de la lepra en las Américas. [**The Problem of Leprosy in the Americas**] *Bol. Oficina Sanitaria Panamericana*. 1957, June, v. 42, No. 6, 548-56. [39 refs.]

The activities of the Oficina Sanitaria Panamericana (OSP) have so far consisted of gathering information about the amount of leprosy in the various countries and about the resources, human and material, that are available for dealing with it. This organization also appointed an expert who enquired into leprosy in Paraguay, Bolivia, Peru, Ecuador and Colombia in 1951, in Trinidad and Surinam in 1956, and in French Guiana, British Guiana, Guadeloupe, Martinique, St. Lucia and Granada in 1956. A table is shown giving the population; the known, segregated and calculated numbers of leprosy subjects; the numbers of leprosaria and their capacity; the numbers of dispensaries; the dates of information and references. The number of known cases in all adds up to 116,129, and of calculated cases to about 200,000, of which 80,938 are in Brazil, 50,000 in Mexico, 16,000 in Argentina, 12,000 in Colombia, 10,000 in Paraguay (with a population of $1\frac{1}{2}$ million), 6,000 in Cuba, 3,400 in Peru, and 1,000 to 2,000 in the United States.

Ernest Muir

QUAGLIATO, R. Lepra conjugal. Estudo epidemiológico dos casos observados no Dispensário do D.P.L. em Campinas, S.P. (1934-1954). [**Conjugal Leprosy. Epidemiological Study of Cases observed in the Dispensary of the Department of Prophylaxis of Leprosy in Campinas São Paulo**] *Rev. Brasileira Leprologia*. S. Paulo. 1957, Jan.-Mar., v. 25, No. 1, 59-68. English summary.

Out of 7,062 contacts of leprous patients examined 500 had contracted the disease. 7.8% of 639 in contact with leprous spouses had contracted

leprosy, compared with 9.9% in 2,064 children, 9.0% in 400 parents, 8.8% among 1,365 brothers and sisters, and 3.3% among 2,594 others. 30% of the spouses had been examined regularly (at least once each year) against 16% for brothers and sisters, 23% for children, and 25% for parents. These figures were gathered from the records of the leprosy dispensary at Campinas covering the period 1934 to 1954. All the patients who infected their spouses suffered from the lepromatous type of leprosy.

Ernest Muir

HANKS, J. H. **Quantitative Aspects of Sampling Leprosy Skin Lesions by the Scraped Incision Method.** *Internat. J. Leprosy.* New Orleans. 1956, Oct.-Dec., v. 24, No. 4, Pt. 1, 424-33, 2 figs.

Experiments were done in order to obtain a method of estimating the numbers of *Myco. leprae* in scrapings from skin incisions. At present, mistakes are made by spreading a small quantity of material over too large an area of the slide surface. Thus the area covered should be proportional to the amount of material. By increasing the thickness of the film to 4 times that recommended for routine purposes it can be made 14 times more sensitive. In order to prepare uniform films it was found best to spread the sample to the greatest extent which permits "a natural redistribution of cellular components" to take place before drying begins. Films made 4 times the baseline density increased the possibility of finding bacilli by a factor of $2.6 \times$. To prevent loss of cells and bacilli during decolorization of carbol-fuchsin-stained films, dilute sulphuric acid containing methylene blue is recommended.

Ernest Muir

TANIMURA, T., HONDA, H. & OSHIMA, T. **Studies on the Serology of Leprosy. The Complement-Fixation Reaction by a Modified Antigen. The Handai Method (Honda).** *Internat. J. Leprosy.* New Orleans. 1956, Oct.-Dec., v. 24, No. 4, Pt. 1, 434-46, 6 figs. [25 refs.]

In order to find an antigen with high sensitivity with various types of leprosy but low sensitivity with other sera, crude cephalin was fractioned by Folch's method and the 3 components were tested with pooled sera from lepromatous cases. The optimal combination of the 3 components was: cardiolipin, cholesterol and cephalin in the ratio of 1:5:10.

With this antigen complement-fixation reactions were positive in 92.4% of lepromatous cases, 73.9% of tuberculoid and 86.4% of neural, there being 96 positives out of 110 cases of leprosy. In 19 tuberculous and 6 cancer cases and in 40 healthy persons the reaction was negative; it was positive in 3 of 38 patients with syphilis, and in 2 out of 10 pregnant women.

The authors believe that this antigen is useful for clinical purposes in leprosy.

Ernest Muir

BECELLI, L. M., DE SOUZA, P. R. & QUAGLIATO, R. Correlação entre os resultados da leitura clínica e do exame histopatológico da reação de Mitsuda. [**Correlation between the Clinical Reading and the Histopathological Examination of the Mitsuda Reaction**] *Rev. Brasileira Leprologia*. S. Paulo. 1957, Jan.-Mar., v. 25, No. 1, 21-58, 9 figs. [19 refs.] English summary.

The authors studied the clinical readings, comparing them with the histological findings at sites of inoculation 30 days after lepromin injection, in 118 leprosy patients and 21 contacts. They found that in the lepromatous type, when the bacteriological examination had become negative, the lepromin reaction was seldom clinically positive, and that when it was positive there was never a frankly positive (tuberculoid) histological picture. In indeterminate and tuberculoid (whether reactional or not) types, and in non-lepromatous contacts, the lepromin reaction was, histologically, frankly or at least slightly positive in cases with clinical lepromin readings of 1+ or 2+. In all cases of tuberculoid type, whatever the strength of the clinical reading (1+, 2+, or 3+), the reaction was never negative histologically; and this was in marked contrast to lepromatous cases which had become bacteriologically negative, and in which a positive clinical reading was accompanied by a negative histological picture.

The authors believe that in non-lepromatous cases doubtful clinical and histological readings may indicate a certain degree of resistance in about one-third of patients; and that histologically 1+ and 2+ reactions are indistinguishable and have the same prognostic value. A matter for discussion is whether the present 1+ and 2+ readings should be classed together as 1+, and the present 3+ reading be classed as 2+. In bacteriologically negative lepromatous cases the lepromin reaction should not be considered positive on clinical reading alone, without histological confirmation.

Ernest Muir

LOWE, J. & DAVEY, T. F. **Tuberculin and Lepromin Reactions in Nigeria. An Analysis of the Data of Lowe and McNulty.** *Internat. J. Leprosy*. New Orleans. 1956, Oct.-Dec., v. 24, No. 4, Pt. 1, 419-23.

LOWE and McNULTY, at the time of writing the paper referred to [this *Bulletin*, 1953, v. 50, 948], did not know of non-specific reactions to large doses of tuberculin. For this reason, and because of the particular interest of the relationship between tuberculosis and leprosy in a country where leprosy is diminishing and tuberculosis increasing, the data are submitted for further analysis.

With two strengths of tuberculin (von Pirquet (equivalent to 10 TU) to elicit strong reactors, and in those negative to this, Mantoux 50 TU to find out weak reactors) the authors tested 2 groups for sensitivity to

tuberculin, one being healthy adults and the other healthy children. Out of 278 healthy adults 79 showed high sensitivity to tuberculin, and of these 76 were found to be lepromin positive; 144 had low sensitivity and of these 121 were lepromin positive; 55 were insensitive to tuberculin and of these 27 were lepromin positive. Thus there was close association between high sensitivity to tuberculin and positivity to lepromin, and many with positive lepromin reaction showed a low sensitivity to tuberculin. Out of 81 healthy children 10 (about half the proportion of the adults) showed high sensitivity to tuberculin and of these 9 were lepromin positive; 37 had low sensitivity and of these 22 were lepromin positive; 34 were insensitive to tuberculin and of these none were lepromin positive. Among the children 58% were tuberculin positive, a higher proportion than in an industrial area in England; and yet these children had practically no chance of exposure to tuberculosis. They had had much more chance of infection with leprosy, and that is considered a more likely cause of their sensitivity to tuberculin.

The adults in the experiment were largely educated people connected with a college, and therefore not typical of the general population of Eastern Nigeria, but it is hoped to carry out further trials among the settled population where leprosy has been known and followed for some years.

The authors refer to tuberculin tests made more recently in 321 lepromatous patients, many of them early cases. 103 (32.2%) gave positive reactions to the von Pirquet test. These findings indicate "that in approximately one-third of all the lepromatous cases encountered during this period a high degree of sensitivity to tuberculin was unable to induce any corresponding sensitivity to lepromin". It is doubted if BCG could have achieved anything different. This "specific inability" of lepromatous leprosy patients to become sensitized to lepromin is being studied further.

Ernest Muir

WADE, H. W. **The Lepromin Reaction and Nonspecific Reactivity to Tuberculin.** [Editorial.] *Internat. J. Leprosy*. New Orleans. 1956, Oct.-Dec., v. 24, No. 4, Pt. 1, 464-72. [Refs. in footnotes.]

This editorial comments on the papers by LOWE and McNULTY, LOWE and McFADZEAN, and LOWE and DAVEY [this *Bulletin*, 1953, v. 50, 948; 1954, v. 51, 278; 1957, v. 54, 49; above, p. 1194]. The author finds that people who react to small doses of tuberculin, that is with specific reactivity, are the most reactive also to lepromin, that those who require larger doses of tuberculin to cause reaction and who have non-specific sensitivity are less likely to be lepromin positive, while those with completely negative reaction to tuberculin have the smallest proportion of positive lepromin tests.

The question is asked whether lepromin positivity associated with this

non-specific sensitivity to tuberculin is related to resistance to leprosy infection in the same way as is natural or spontaneous lepromin positivity. The author then reiterates his belief that the Mitsuda test "is one of capability to react to the dose of lepromin injected because of immunological changes induced by the injection of the lepromin, which is an allergen". He adds, however, that the basic capability of reacting may be enhanced by non-specific means so that people who would not otherwise react to a single injection of lepromin may do so, and others may react more strongly.

Mention is also made of the work of the Medical Research Council who found that on follow-up the incidence of tuberculosis among high-dose reactors was 0.74 per thousand, compared with 1.75 among the low-dose reactors who presumably had been sensitized by infection with the tubercle bacillus.

The editorial finishes with a reference to the work of DHARMENDRA and CHATTERJEE [*ibid.*, 1955, v. 52, 1093]. Ernest Muir

CONVIT, J., SISIRUCA, C. & LAPENTA, P. **Some Observations on Borderline Leprosy.** *Internat. J. Leprosy.* New Orleans. 1956, Oct.-Dec., v. 24, No. 4, Pt. 1, 375-81.

Of 8,872 known cases of leprosy in Venezuela in 1956, 286 were of the borderline form. Of the latter patients 100 were admitted to hospital and studied. There were 68 with reactive disease who are divided according to the state of their general health, and 32 non-reactive patients of whom 10 had diffuse and 22 plaque-like lesions. Clinical, bacteriological, immunological and histological tests were made in all cases. In 63% there was an easily-recognized, bat-like appearance of the face (*facies dimorpha*). In 27% there was a hypochromic halo, interpreted as a sign of regression, beginning peripherally and spreading inwards, though in some it seemed to be a disturbance of pigmentation due to centrally-placed very active lesions. There were also in 61% of cases hypopigmented patches secondary to infiltrated lesions, which have carefully to be distinguished from the indeterminate group. These patches may regain their pigment or may persist for a long time; they may become erythematous, transform into the tuberculoid (infrequent) or into the lepromatous type, and may spread centrifugally. The tests for sensation and the histamin test vary and may be dissociated.

Tests with methylene blue were found useful, not so much in studying cases of pure borderline leprosy but particularly where there were patches of lepromatous type interspersed with borderline. After injections of methylene blue for 1 to 2 or more days lepromatous lesions became intensely blue, but these required more injections if they were distributed inside borderline patches. Borderline lesions did not take on the pigment. Methylene blue was given intravenously in 1% concentration, in daily

doses of 3 cc. rising to 10 cc. on the 15th day. The dose of 10 cc. was continued in those without coloured lesions even as long as 4 months.

[This paper throws considerable new light on a form of leprosy which is often very imperfectly understood.]

Ernest Muir

SATO, S. **Nerve Abscess in Lepromatous Leprosy. Report of a Case, with a Review of Reports of Nerve Abscess in Japan.** *Internat. J. Leprosy*. New Orleans. 1956, Oct.-Dec., v. 24, No. 4, Pt. 1, 408-18, 6 figs. on pl. & 1 text fig. [30 refs.]

Nerve abscesses, though not infrequent in India, are apparently uncommon in Japan, where 4 occurring in 3 cases of lepromatous leprosy and only 13 in the tuberculoid type are recorded in the literature. One of the former cases is described by the author.

There were several thickened nerves and cherry-sized abscesses in 2 nerve branches in the neighbourhood of the ulnar nerve. These contained whitish-yellow pus in which smears showed abundant leprosy bacilli with globi. "The nerve cord as a whole is changed into a lepromatous granuloma . . . consisting of lepra cells in various stages of evolution including numerous large foamy cells."

Another case, that of HIRAKO, is of particular interest: "The patient had lepromatous leprosy which at the time was in the 'secondary neural' state. Abruptly, in a night, there appeared on all four extremities many small subcutaneous nodules—abscesses—that varied in size from a grain of rice to a kernel of corn. These corresponded to the superficial branches of nerves, such as the antebrachial, ulnar and sural. . . . Caseous necrosis with a wall of foamy cells and histiocytes in the nerve was the main histological finding in the nodules". It was concluded that necrosis of lepromatous granuloma was the cause of the abscess formation.

Ernest Muir

HUGON, J. & PIERON, A. **Trois ans de traitement au D.A.D.P.S. en milieu rural. [Three Years of Treatment with DADPS [DDS] in a Rural Region]** *Ann. Soc. Belge de Méd. Trop.* 1957, Feb. 28, v. 37, No. 1, 71-89. [10 refs.]

Oral treatment with DDS was found best in hospitals, but was unsuitable for mass dispensary treatment. Preference was given by the authors, working in the Belgian Congo, to a suspension of DDS in chaulmoogra esters. After 700 patients had been treated with injections of these suspensions, twice each month, in a dosage of 5 cc. containing 1.25 gm. of DDS for a period of 3½ years, 248 of them [192 indeterminate, 56 tuberculoid] were carefully examined. It was found that there were striking cures in 40% and remarkable improvement in 45%. Among side effects there was a case of exfoliative dermatitis, one of hepatitis and one of agranulocytosis, all of these being fatal. There was also a suicide.

However, these serious accidents are not considered as important drawbacks to the treatment, considering the slight medical supervision that was possible. Puncture biopsies of the liver showed changes in some cases which were ascribed to the treatment.

Ernest Muir

VAN DER MEULEN, G. & MELEN, G. Communication des résultats du recensement de la lèpre et son traitement ambulatoire en secteur de Banalia. [**Report on a Survey of Leprosy and its Ambulatory Treatment in a Part of Banalia**] *Ann. Soc. Belge de Méd. Trop.* 1957, Feb. 28, v. 37, No. 1, 115-22.

In the area described leprosy was found in 6.6% of the population; among 3,083 patients found with leprosy 82% had the tuberculoid type and 16.2% the lepromatous. Treatment was begun with oral DDS, but this was abandoned for injections of a suspension, 2.5 cc. being given once a week, and again later changed to 5 cc. (representing 25 mgm. of active sulphone per kgm.) every second week. About 80% of regular attendances were obtained.

Of patients under treatment for more than 2 years there was apparent cure in 21.7% of tuberculoid cases, in 5.5% of lepromatous, and in 4.16% of indeterminate cases. In less than 2 years there was cure of 13.71% tuberculoid and 4.51% lepromatous patients. There was, however, clinical amelioration in 60 to 70% of patients.

Ernest Muir

KINNEAR, A. A. **The Excretion of N'-Methylnicotinamide and N'-Methyl-2-Pyridone-5-Carboxylamide in Leprosy and the Response to DDS Therapy.** *South African J. Lab. & Clin. Med.* 1957, Mar., v. 3, No. 1, 63-6, 1 fig. [17 refs.]

The present investigation deals with excretion of metabolic products of niacin (nicotinic acid) in the urine of 20 patients with lepromatous leprosy and 20 with tuberculoid leprosy before and after treatment with DDS. Similar estimations were made on the urine of normal patients. The two products estimated were those described in the title. N'-methylnicotinamide is apparently converted to the pyridone derivative in the liver. In pilot experiments the amounts recovered amounted to as much as 80% of the nicotinamide administered. Leprous patients, especially those with lepromatous lesions, excreted less of these two substances than normal patients. After 1 year's treatment with DDS, however, there was little change in the amounts excreted, except possibly for a small increase in N'-methylnicotinamide in the case of tuberculoid patients. It has not been proved that the low excretion of these substances during the course of the disease is due to increased demand. An added interest of the niacin structure is that it occurs in co-enzymes I and II.

J. D. Fulton

LEIKER, D. L. **The Mononucleosis Syndrome in Leprosy Patients treated with Sulfones.** *Internat. J. Leprosy.* New Orleans. 1956, Oct.-Dec., v. 24, No. 4, Pt. 1, 402-5.

A condition is described in 3 patients similar to what was described in 1949 by LOWE and SMITH as "glandular fever and exfoliative dermatitis precipitated by sulphones" [this *Bulletin*, 1950, v. 47, 474]. Two of the present cases were very severe, the mononuclears going up to 70% and 86% and the second patient dying. The author doubts the diagnosis of infectious mononucleosis, and considers it more likely to be an "allergic reaction of the reticuloendothelial system induced by sulphones and other drugs". Three reasons for this diagnosis are: infectious mononucleosis has not been found in Netherlands New Guinea, apart from the treatment of leprosy; the syndrome occurs only during the early treatment of leprosy and not later; 2 of the 3 patients were immediately relieved with cortisone.

Ernest Muir

VALETTE, A. Antihistaminiques et réactions lépreuses. [**Antihistamines and Lepra Reactions**] *Bull. Soc. Path. Exot.* 1957, Mar.-Apr., v. 50, No. 2, 200-203.

The author, after trying out various remedies for the lepra reaction caused by sulphone treatment, discarded most of them because they were ineffective, and others such as cortisone because of the expense and need of clinical attention. He found, however, that histopyrrodine, the hydrochloride of pyrrolidyl-ethyl-phenyl-benzylamine, sold under the name of Domistan, was more effective. He used this antihistamine, giving orally 2 tablets of 25 mgm. each twice a day, in 46 patients of whom 39 were lepromatous and 7 tuberculoid. In 43 patients the cutaneous and general signs of reaction disappeared within 4 to 6 days, without the need to interrupt sulphone treatment.

Histopyrrodine may also be used as a preventive (2 tablets daily) in lepromatous patients likely to have reactions at the beginning of sulphone treatment.

The advantages of this drug are its effectiveness, non-toxicity, absence of soporific effect and the low price. These qualities make it particularly suitable for mass treatment.

Ernest Muir

DAVISON, A. R. **Clinical Evaluation of Isonicotinic Acid Hydrazide as Adjuvant in the Treatment of Lepromatous Leprosy with a Note on the Detrimental Effect of Erythema Nodosum Leprosum Reactions.** *Internat. J. Leprosy.* New Orleans. 1956, Oct.-Dec., v. 24, No. 4, Pt. 1, 393-401, 3 figs.

4 groups of patients with lepromatous leprosy were tested over a period of 2 years: (A) 40 patients on sulphone alone (maximum 200 mgm. daily)

acted as a control group; (B) 40 were given sulphone plus isoniazid 500 mgm. 6 days a week; (C) isoniazid and dihydrostreptomycin 1 gm. injected twice weekly, plus PAS with a maximum dose of 30 tablets of 0.5 gm. daily, were given to 39 patients; (D) streptohydrazid (streptomycin 1 gm. and isoniazid 266 mgm. in 1 molecule) 1 dose injected twice weekly in 10 patients. The improvement in group A was 46%, in B 41%, in C 47% and in D 51%. "The degree of improvement was therefore almost equal with all of the four treatments."

Erythema nodosum was considered to be a disadvantage when it occurred; out of 58 cases without this reaction there was 42% reduction in the bacteriological index, whereas in 59 cases with reaction there was only 12% reduction. "The possible value of the corticosteroids in this connection should be considered."

Ernest Muir

LARA, C. B., PALAFOX, C. A., IGNACIO, J. L. & NOLASCO, J. O. **Children of Leprosy Patients isolated at Birth, given Lepromin and BCG Injections, then returned to the Colony, First Report.** *Internat. J. Leprosy*. New Orleans. 1956, Oct.-Dec., v. 24. No. 4, Pt. 1, 382-92.

At first, children born in the Culion Colony were sent to an orphanage in Manila. This was unsatisfactory to the parents, and a Children's Home was built just outside the colony. Children, however, were not separated from their parents till the age of 6 months, that being then considered the age at which to separate them to avoid the danger of infection. Isolation at birth was not attempted from fear of high mortality. The results of these measures have been reported in various articles [see this *Bulletin*, 1956, v. 53, 1430]. After the war the first attempt was made to isolate the children at birth, after which they were to be divided into 3 groups: one group to remain permanently in a non-leprous environment, another to be returned to the parents after a period, and a third to be returned only after the lepromin test had been made strongly positive through repeated testing.

Of 100 children isolated from birth in a Culion nursery, excluding 1 who died at 10 days of a congenital head defect, 11 were sent outside Culion, 55 whose lepromin reaction had been rendered moderately or strongly positive by BCG inoculation or by repeated lepromin testing were returned to their parents in the Colony, while 33 still remained in the nursery in March 1956. In assessing results the authors point out that the numbers are too small and the time still too short to warrant any definite statement as to the value of BCG in increasing the Mitsuda reaction. Also there is the question to what extent such increase is promoted by the repeated injections of the lepromin in carrying out the tests. Of the 55 children returned with positive reactions to the colony 46 have now been exposed to infection for 12 to 18 months without showing evidence of infection.

but 3 more years will be required before any assessment can be made of the "protective value of prolonged isolation from birth and the effects of lepromin injections and BCG vaccinations".

Ernest Muir

KÁTÓ, L. & GÖZSY, B. **Action of Histamine and Antihistamine on the Ingestion of Murine Leprosy Bacilli by Macrophages of the Rat and the Guinea-Pig.** *Internat. J. Leprosy.* New Orleans. 1956, Oct.-Dec., v. 24, No. 4, Pt. 1, 447-56, 6 figs. on pl. [13 refs.]

"Phagocytosis of the tubercle bacillus of a BCG culture, and of the murine leprosy bacillus of a leproma suspension, by macrophages of glycogen-induced peritoneal exudates of guinea-pigs and albino rats was studied to determine the influence of histamine and an antihistamine (mepyramine maleate). Ingestion of BCG by the cells of both species was stimulated by histamine and inhibited by the antihistamine. On the other hand, phagocytosis of the murine bacillus was not influenced by either of the two substances, this contrary result being obtained with both kinds of exudate cells. A raw, bacillus-free, aqueous extract of the rat leproma inhibited phagocytosis of BCG by the guinea-pig monocytes. The active substance is considered responsible for the monopolization of the monocytes by *M. leprae murium*. The rat leproma extract and the antihistamine induce similar morphological and functional alterations of the monocytes; absence of pseudopodia and vacuoles, shrinkage of the cell, and a passive behavior with regard to BCG."

HELMINTHIASIS

In this section abstracts are arranged as far as possible in the following order:—TREMATODES (schistosomes, other flukes); CESTODES (Diphylobothrium, Taenia, Echinococcus, other cestodes); NEMATODES (Hookworms, Ascaris, Filarial worms, Dracunculus, etc., Trichuris, Enterobius, Trichinella, etc.).

OKPALA, I. **Diagnosed Cases of Schistosomiasis in Lagos (Nigeria) 1951-1955.** *West African Med. J.* 1957, June, v. 6 (n.s.), No. 2, 74-8, 1 graph.

Between 1951 and 1955 some 14,000 specimens of urine found to contain protein were examined microscopically. 661 (4.7%) of these contained *Schistosoma haematobium* eggs; 529 (80%) of the infected specimens were from male patients and 132 (20%) from female. There were 38 children and infants in this total. Of some 29,000 stools examined during the same period 17 were found to contain *S. mansoni* eggs; 12 were from

male patients and 5 from female. Schistosomiasis, whether imported or locally acquired, is therefore a public health problem of importance in Lagos.

A. R. D. Adams

EDINGTON, G. M. **Schistosomiasis in Ghana with special reference to its Pathology.** *West African Med. J.* 1957, June, v. 6 (n.s.), No. 2, 45-57, 4 pls. [27 refs.]

Schistosomiasis, both that due to *Schistosoma haematobium* and that due to *S. mansoni*, is widespread in Ghana. There is little knowledge of its effect on the local morbidity and mortality rates as the literature on the subject locally is conflicting. A record of the incidence of the diagnosed infections in hospital patients in various areas shows that *S. haematobium* infection generally is by far the most frequent, though the incidence of *S. mansoni* infection in hospital patients from Kumasi was only rather less than half that of the other parasite, and in those from Bawku, Northern Territory, the figures of incidence of the two closely approximated.

Biopsy records between 1943 and 1955 and autopsy records between 1923 and 1955 from the Medical Research Institute of Accra have been studied by the author. The former records (29 positive in over 7,000 specimens) did not suggest that schistosomiasis was an important cause of morbidity in Ghana; the autopsy records proved of little value in assessing the mortality due to this condition. During 1955 records of autopsies on all patients (24) dying of uro-genital disease were examined; in 9 of these cases schistosomiasis was considered to be the primary cause of disease. Schistosomiasis was held, at autopsy, to be the cause of death in 2.1% of 427 patients who had died naturally in Accra in this year; the corresponding figure for cerebral malaria was 1.2%. Some details are given of the distribution of the schistosomal lesions and their consequences in these patients; cirrhosis of the liver and enlargement of the spleen were not among them. The apparently high incidence of mortality found to be due to schistosomiasis was unexpected in view of the apparently low morbidity attributable to the condition in Accra.

A. R. D. Adams

ISHAK, K. G., HAZZI, C., SALIB, M., SABOUR, M. & MAHROUS, A. R. **Needle Biopsy in the Etiologic Diagnosis of Splenomegaly.** *Amer. J. Trop. Med. & Hyg.* 1957, Mar., v. 6, No. 2, 257-65, 8 figs. on 4 pls. [18 refs.]

The authors, seeking to establish the aetiology of splenomegaly in Egyptians suffering from schistosomiasis ("Egyptian splenomegaly"), have obtained biopsy specimens of the splenic pulp from 55 patients with this syndrome by using the Vim-Silverman needle. Both the trans-thoracic and the transabdominal route were used, though the latter was

preferred. No further details of the puncture technique are given and no complications or untoward sequelae are mentioned: there were no deaths in this series and the procedure is considered to be safe. Thin smears of splenic pulp were made at the time of biopsy in cases in which a detailed cytological examination was indicated; otherwise the material was sectioned.

It is of interest to note that the spleen in cases of schistosomal fibrosis of the liver showed only non-specific congestive changes indistinguishable from those seen in other types of cirrhosis, nor was the presence of an excess of eosinophil leucocytes a specific sign of this infection. An example of miliary tuberculosis and two examples of Gaucher's disease were recognized by this technique.

[The work described is praiseworthy in that it facilitates the classification of cases hitherto grouped in a clinical syndrome which has never merited a specific name. In the absence of detailed information on technique, however, it is doubtful whether many clinicians will be sufficiently bold to adopt this procedure.]

J. H. Walters

NAGATY, H. F., MOAWAD, M. B. & SALEM, S. **Papular Skin Lesions in which Schistosome Eggs were found.** *Amer. J. Trop. Med. & Hyg.* 1957, Mar., v. 6, No. 2, 266-70, 3 figs.

The authors, in Egypt, saw a girl of 12 years who 7 years previously had been treated, inadequately, for urinary schistosomiasis. One morning, 6 years later, she suffered burning sensations in the skin of the trunk, neck, thighs and arms, and red itching papules developed within some hours; within a few days these became vesicles, and then pustules; the pustules ulcerated and discharged a greenish pus for about a month, leaving keloid swellings. *Schistosoma haematobium* eggs were found in the urine; there was a 44% eosinophilia in a total count of 13,600 leucocytes per cmm.; a radiogram of the chest was of normal appearance. Biopsy of an affected piece of skin showed a granulomatous focus containing a *S. haematobium* egg. Specific schistosomicidal treatment, after a brief exacerbation of the lesions, resulted in their eventual disappearance.

A. R. D. Adams

SACRE, J. & DUBOIS, A. Subocclusion intestinale à *Schistosoma mansoni*. [**Intestinal Subocclusion due to *Schistosoma mansoni***] *Ann. Soc. Belge de Méd. Trop.* 1957, Feb. 28, v. 37, No. 1, 147-50, 2 figs. on pl.

The English summary appended to the paper is as follows:—

“A case of intestinal subocclusion in a child of 10 years. The severity of the general and local condition and the possibility of the existence of a tumor lead the author to proceed to the resection of the colon. The histopathological picture ascribes the syndrome to *Sch. mansoni*.”

CHERNIN, E. & MICHELSON, E. H. **Studies on the Biological Control of Schistosome-Bearing Snails. III. The Effects of Population Density on Growth and Fecundity in *Australorbis glabratus*.** *Amer. J. Hyg.* 1957, Jan., v. 65, No. 1, 57-70, 4 figs. [16 refs.]

Groups of *Australorbis glabratus* of similar shell diameter were maintained in 10-litre glass tanks under standard conditions of aeration, temperature, light and substrate. Watercress was provided as food and was replenished as required. The only variable in the tanks was the number of snails.

In the first experiment where the mean diameter of the snails in 3 tanks was 7.4, 7.2, 7.4 mm., measurements made on the 11th, 18th and 25th day showed that the snails in the tank with a population of 20 grew appreciably faster than those in a population of 150, while the diameter of the shells of snails in the 50 population were intermediate in size. In another experiment where snail diameter ranged between 0.7 and 1.0 mm., the population size was 60 and 620 per tank. Similar retardation of growth was observed in the more heavily populated tank. In a third experiment 2 tanks each containing 25, 50, or 150 snails were set up. In one tank of each pair the egg masses laid during the course of the experiment were allowed to hatch; in the other they were removed. It was found that in the populations of snails of similar size these grew equally, that the rate of growth in the more heavily populated tanks was markedly retarded and that the mean number of eggs per snail, the mean number of eggs per mass and the mean number of egg masses per snail all decreased as population density increased. In a fourth experiment where water analysis was carried out after 30 days no significant difference in chemical or physical properties was found in aquaria that had contained 50 or 150 snails.

O. D. Standen

CHERNIN, E. & MICHELSON, E. H. **Studies on the Biological Control of Schistosome-Bearing Snails. IV. Further Observations on the Effects of Crowding on Growth and Fecundity in *Australorbis glabratus*.** *Amer. J. Hyg.* 1957, Jan., v. 65, No. 1, 71-80, 5 figs.

This series of experiments differed mainly from those described by the same authors [above] in that groups of *Australorbis glabratus* of equal diameter and equal in number were cultured in different volumes of distilled water. In some experiments unexpected results were obtained in that groups of snails in one volume of water grew faster than those in twice or half that volume and that snails in the smallest volume demonstrated the greatest fecundity. In a further experiment 25 snails in 5 litres of tap water grew more rapidly than 50 in 10 litres, 5 litres or 2.5 litres. In a third experiment in tanks with volume constant but with different population densities the snails showed faster growth and greater fecundity where the population density was lowest. Where population

density remained equal but volume of water varied the results were much as in the earlier experiments of the series. Where the water volume per snail was equal but the population numbers per tank were different the snails in the numerically smaller group grew faster than those in the larger group. In all experiments, mortality rate was not related to population density.

"It is concluded that . . . no one hypothesis suffices to explain the relationship observed."

O. D. Standen

DEWITT, W. B. **Experimental Schistosomiasis mansoni in Mice maintained on Nutritionally Deficient Diets. I. Effects of a *Torula* Yeast Ration Deficient in Factor 3, Vitamin E, and Cystine.** *J. Parasitology*. 1957, Apr., v. 43, No. 2, 119-28, 6 figs. (4 on pl.). **II. Survival and Development of *Schistosoma mansoni* in Mice maintained on a *Torula* Yeast Diet deficient in Factor 3, Vitamin E, and Cystine.** *Ibid.*, 129-35, 6 figs. on pl.

I. Mice were maintained on a *Torula* yeast diet which is deficient in Factor 3, vitamin E and cystine and which produces liver necrosis and also necrotic degeneration of the heart, muscle and kidneys and atrophy of the pancreas and testicles; the mice die in 65-70 days. The mice were infected with *S. mansoni*, but in these deficient hosts the growth of the worms was stunted so that they did not attain normal adult size or sexual maturity. Consequently no eggs were produced and this major cause of lesions was absent.

The deficient diet also produced considerable alterations in the serum proteins, *viz.*—14% decrease in total protein, 23% decrease in albumin, no change in alpha globulin, 20% increase in beta globulin, 50% decrease in gamma globulin and 26% decrease in the A/G ratio. *S. mansoni* infection produced no alteration in the serum proteins of such deficient animals, although in well-fed mice it caused an increase of gamma globulin from 0.4 gm.% to 1.5 gm.%. Apparently the deficient animals are unable to respond to the infection or the underdeveloped worms are incapable of producing an adequate stimulus.

In the deficient animals the coagulation time of the blood was increased from 2.7 to 5.5 minutes; prothrombin time was increased from 12 to 26 seconds and the fibrinogen levels fell from 0.33 gm.% to 0.19 gm.%. It is not known whether the different response of indigenous populations to schistosomiasis in different parts of Africa may be due, in part, to differences in the diet.

II. In this work the mice were exposed to 150 cercariae each, either when they were weaned and placed on the diet, or when they had been on the diet for 4 weeks. They were killed and examined 8 weeks after infection. Compared with the control mice on a normal diet, the deficient mice harboured 69% more worms; thus the deficient diet diminished the natural resistance of the host. The somatic development of the worms

was much impaired and most of them did not reach sexual maturity. The length of female worms posterior to the ovary was more severely affected than that anterior to the ovary. Eggs (when present) were abnormal, being pigmented and highly granular. The male worms were as severely stunted as the female worms. All these changes could be prevented by supplementing the diet with Factor 3 or with vitamin E plus cystine.

[See also KRAKOWER *et al.*, this *Bulletin*, 1942, v. 39, 562; 1945, v. 42, 133.]

F. Hawking

WATANABE, H. **The Clinical and Pathohistological Study on the Schistosomiasis Patients diagnosed by Liver Biopsy.** *Kurume Med. J.* 1956, v. 3, No. 3, 169-83, 9 figs. [22 refs.]

YOSHIZUMI [this *Bulletin*, 1955, v. 52, 662; 1956, v. 53, 617] demonstrated the efficacy of needle biopsy of the liver and immediate examination of the fresh material so obtained for the diagnosis of *Schistosoma japonicum* infections. The author has followed this technique, and has made parallel histological studies of the liver. He deals diffusely and discursively with symptoms, associated disorders, complications, and the treatment of Far Eastern schistosomiasis. He concludes that puncture biopsy is safe and that it is 8 to 9 times as effective in the diagnosis of Far Eastern schistosomiasis as is stool examination. Complicating disease may obscure the clinical diagnosis and render the subsequent treatment more difficult. Cirrhosis of the liver is a common sequel of this disease.

A. R. D. Adams

T'AO, Shou-Ch'i. **Cardiac Manifestations of the Toxic Action of Potassium Antimony Tartrate in Schistosomiasis Patients. Paroxysmal Ventricular Tachycardia and Fibrillation.** *Chinese Med. J. Peking.* 1957, May, v. 75, No. 5, 365-78, 5 figs. on 4 pls. [28 refs.]

Potassium antimony tartrate, in spite of its recognized dangers, is widely used for the treatment of all forms of schistosomiasis. The organs probably most affected by the drug are the liver and the heart. Many workers have reported on its effects on the latter organ, but most consider that the changes are transitory and do not indicate serious damage to the heart or impairment of its function. Thousands of patients in China lately have been treated with tartar emetic for Far Eastern schistosomiasis; toxicity in the form of the Adams-Stokes syndrome is not infrequent among these and it may be fatal. During the last year the author himself has seen 4 cases of serious ventricular arrhythmia of this origin. He gives full details of these, with plates showing the electrocardiographic recordings from each. These 4 patients were young (19 to 28 years) and none had evidence of antecedent heart disease. Premonitory symptoms and signs of the onset of the condition were negligible.

The author concludes with the following summary:—

“1. Four cases of paroxysmal ventricular tachycardia, flutter and fibrillation developing in patients under treatment with potassium antimony tartrate for schistosomiasis japonica are reported. Two patients recovered and 2 died after repeated Adams-Stokes seizures.

“2. The electrocardiographic picture in the prefibrillatory period has been described, and the relationship between preliminary changes in the basic ventricular deflections and the development of ventricular fibrillation discussed.

“3. It is believed that ventricular arrhythmias of the type reported constitute the main cause of occasional deaths in patients receiving therapeutic doses of potassium antimony tartrate. They assume great importance in an extensive program of treatment of large number of patients with schistosomiasis. The factors responsible for the unusual susceptibility to the toxic action of the drug in a small percentage of patients are not entirely clear.

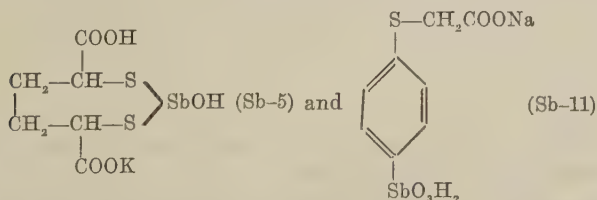
“4. The experience gained from the cases here reported bears out the validity of the current clinical conception that ventricular fibrillation may occur in a transient recurrent form that can be fatal or end in recovery. The difficulty in the management of such cases is pointed out.”

A. R. D. Adams

CHU, Chiao-Chen, TSEN, Yea-Lin, LIANG, Yu-I & TING, Kuang-Sheng.
[Studies on Antibilharzial Drugs. IV. Experimental Therapy of
12 New Compounds given Intraperitoneally in Mice] Reprinted from
Acta Physiologica Sinica. 1957, v. 21, No. 1, 12-18. [10 refs.]
[In Chinese.]

The English summary appended to the paper is as follows:—

“Intraperitoneal injections of 6 stibonic acids and their relative compounds derived from sulfa-drugs, 3 dithiastibiols, 2 organotin compounds and 1 organomercury compound were studied for their therapeutic activities against schistosomiasis japonica in white mice. The LD₁₀, LD₅₀, or the minimal lethal doses were used for treatment, which was begun 5 weeks after exposure to 40 cercariae per mouse. The injections were given once daily for 14 days, and, after a holding period of another 14 days, the mice were autopsied. Basing on the average number of worms remained in each mouse, the therapeutic effects of



out of the 12 compounds were better than that of tartar emetic.”

LIANG, Yu-I, TSEN, Yea-Lin, CHU, Chiao-Chen & TING, Kuang-Sheng.
[Studies on Antibilharzial Drugs. V. Combined Therapy with Procaine and Tartar Emetic] Reprinted from *Acta Physiologica Sinica*. 1957, v. 21, No. 1, 19-23. [12 refs.] [In Chinese.]

The English summary appended to the paper is as follows:—

“(1) In white mice, intraperitoneal injections of mixture of procaine (70 mg/kg/day) and tartar emetic for 14 days reduced the toxicity of tartar emetic, raising the LD₅₀ of the latter from 35 to 45 mg/kg/day.

“(2) This detoxication effect is primarily due to procaine *per se*, not due to its hydrolytic products (PABA and DEAE).

“(3) In guinea pigs, procaine showed no protection against the acute mortality from tartar emetic.

“(4) In rabbits infected with *Schistosoma japonicum*, intravenous injections of mixture of procaine (10 mg/kg/day) and tartar emetic for 14 days could increase the therapeutic activities of tartar emetic. Injections of mere procaine showed no antibilharzial effect.”

LIANG, Yu-I, CHU, Chiao-Chen, TSEN, Yea-Lin & TING, Kuang-Sheng.
[Studies on Antibilharzial Drugs. VI. The Antidotal Effects of Sodium Dimercaptosuccinate and BAL-Glucoside against Tartar Emetic] Reprinted from *Acta Physiologica Sinica*. 1957, v. 21, No. 1, 24-32, 1 chart. [19 refs.] [In Chinese.]

The English summary appended to the paper is as follows:—

“(1) On single intraperitoneal injection to white mice, the LD₅₀ levels of BAL-glucoside and Na $\alpha\alpha'$ -dimercaptosuccinate were found to be 5660 and 2730 mg/kg respectively.

“(2) Hypodermic administrations of sublethal doses of BAL, BAL-glucoside or Na $\alpha\alpha'$ -dimercaptosuccinate could significantly reduce the toxicity of tartar emetic given intraperitoneally in mice. BAL (40 mg/kg), BAL-glucoside (2500 mg/kg) and Na $\alpha\alpha'$ -dimercaptosuccinate (1500 mg/kg) raised the LD₅₀ of tartar emetic from 31 to 52, 85 and 491 mg/kg respectively. Thus Na $\alpha\alpha'$ -dimercaptosuccinate appeared to far exceed any antidote reported in the literature.

“(3) Within 8 hours after intravenous injection of lethal dose of tartar emetic (20 mg/kg) in rabbits, administrations of BAL, BAL-glucoside or Na $\alpha\alpha'$ -dimercaptosuccinate were all able to protect or prolong the life.

“(4) The therapeutic activity of tartar emetic against schistosomiasis japonica in mice was diminished by all these 3 dimercaptans, among which Na $\alpha\alpha'$ -dimercaptosuccinate was most powerful, rendering the tartar emetic totally ineffective.”

KAGAN, I. G. & MERANZE, D. R. The Histopathology of the Liver in Mice experimentally infected with *Schistosomatium douthitti*. *J. Infect. Dis.* 1957, Jan.-Feb., v. 100, No. 1, 32-9, 8 figs. on 2 pls. [11 refs.]

In an earlier paper the effect of cercariae of *S. douthitti* upon the skin of mice was described [this *Bulletin*, 1956, v. 53, 341]. In the present paper the pathology of the liver in 78 mice lightly infected with this worm is described. In mice infected with male and female worms, the lesions in the liver were associated with the ova and consisted of the formation of granulomata. The findings were similar to those which other workers have reported to be caused by human schistosomes in experiment animals. [For details the original must be consulted.] In a series of mice infected with female worms in which ova were present, the histological picture was similar to that produced by both sexes. In mice infected only with male worms, the inflammatory response consisted mainly of mononuclear cells around the veins. Apparently the ova are more active than the adult worms in developing the typical histopathology of schistosomiasis. When mice were re-infected 60 days after the first infection there was no enhanced cellular response to the second infection; this suggests that the liver may not be the site of the primary cellular defence of the host during the first 10 days of infection. When mice were cured of their infections, the normal histology of the liver was restored in 270 days. There was no evidence in these experimental animals of schistosomiasis leading to cirrhosis. *F. Hawking*

OYTUN, H. S. Hydatidose in der Türkei. [**Hydatid Disease in Turkey**] *Ztschr. f. Tropenmed. u. Parasit.* Stuttgart. 1957, v. 8, Nos. 1/2, 196-200, 1 map. [17 refs.]

Hydatid disease is widely distributed in Turkey. Both *Echinococcus unilocularis* (*polymorphus*) and *Echinococcus alveolaris* (*multilocularis*) occur in man and animals, the former being much the commoner.

The author examined the records for 1955 of 27 Turkish hospitals and found 220 cases of infection with *E. unilocularis*. Of these 68.1% came from Ankara, 16.4% from Istanbul and 15.41% from other Turkish hospitals. A Turkish author quoted reported on 60 patients, 70% of whom were males, the cysts being commonest in the liver (in 65%), but they were also found in the lungs (in 11.66%) and in muscle, bone, the peritoneum, kidney and other organs. They were commonest in males and in people who worked with animals. Another Turkish author quoted studied the disease in Istanbul and reported that 0.32% of 35,765 patients in an Istanbul clinic had hydatid disease, that in 13,000 surgical operations 0.1% had the disease and that hydatid cysts were found in 0.3% of 3,945 autopsies.

E. alveolaris (*multilocularis*) is much less common, only 11 cases being so far known. References to the Turkish literature on these are given. Cysts of this type were found in the liver, knee-joint, groin and lachrymal sac. A table given by one Turkish author indicates that this type of cyst occurs all over Turkey and is not restricted to certain areas, as it is in Europe.

Hydatid disease is widely distributed in Turkey in sheep, goats, cattle, buffalo, camels and pigs, being commonest in sheep, goats, cattle and buffalo. *E. unilocularis* is predominant in these animals. In the slaughter-houses of large Turkish towns the author found the disease in 50% of the sheep and goats killed. Small echinococci with many cysts, resembling *E. multilocularis* in man, are very rare in slaughtered animals; the author found them in only 1 ox and 1 buffalo. G. Lapage

VOGEL, H. & SCHUMACHER, H. H. Beobachtungen über alveoläre Echinokokken des Zentralnervensystems bei Versuchstieren. [**Observations on Alveolar Echinococci of the Central Nervous System in Experimental Animals**] *Ztschr. f. Tropenmed. u. Parasit.* Stuttgart. 1957, v. 8, Nos. 1/2, 278-87, 6 figs.

FISCHER (*Handbuch Spez. Path. Anat. u. Histol.*, v. 13, II., 1955, Springer) stated that only 31 cases of alveolar echinococcosis of the brain of man are known. RAUSCH and SCHILLER [this *Bulletin*, 1951, v. 48, 661] reported another in an Eskimo in North Alaska. DARDEL (*Das Blasenwurmliden in der Schweiz*, 1927, Bern: A. Francke A.G.), collected 97 cases of echinococcosis in Switzerland, of which 5 (5.4%) involved the brain.

The authors here describe the results of experimental infection of 2 field voles (*Microtus agrestis*) with *Echinococcus multilocularis*, which showed that the brain and spinal cord can be infected in experimental animals, although this is rare as it is in man. These experiments were part of work on 188 mice (the results of which are to be described later), in most of which experimental infection with the eggs of *E. multilocularis* produced an infection of the liver, extending, in some of the mice, into the abdominal cavity, or involving the axilla, thorax or central nervous system; in one mouse the primary infection was in the mediastinum. The eggs were obtained from a dog experimentally infected and the infection originated from a red fox in the Swabian Alps.

The first of the voles described developed paralysis of the hind limbs and was killed 39 days after infection. In the liver there were a number of groups of *Echinococcus* cysts $\frac{1}{2}$ to 2 mm. in diameter and in the right cerebral ventricle there was a group of cysts measuring about 4 mm., which compressed the left cerebral ventricle. The histopathological changes observed in sections are described in detail and for these the original paper must be consulted.

In the second vole no paralysis of the hind limbs was seen, but it may have been overlooked. This vole died 59 days after infection and showed numerous small isolated cysts in the liver, and a large group in the right kidney, much of which was destroyed. There were cysts also on the surface, and in the substance, of the spleen, and a group of cysts about 3 mm. long alongside the vertebral column in the pleural cavity and another about 5 mm. long beside the vertebral column at the level of the

left kidney. This last group had penetrated into the lumbar vertebral column and the sections illustrating the paper show cysts between the roots of the spinal nerves. More caudally there was a marked enlargement and multiplication of the cysts, which here penetrated, especially on the ventral side of the spinal cord, between the nerve roots and pushed the spinal cord dorsally. Other groups of cysts passed through the intervertebral foramina along the spinal nerves and into the perivertebral soft parts, single cysts lying in the tissue spaces and lymph canals of the perivertebral tissues and even in the marrow cavity of a transverse process. Here the cysts caused compression of the nerve roots and of the spinal cord, drawing them dorsolaterally, and many nerve roots showed degenerative changes, as did the ventral part of the spinal cord in its subpial layer.

More caudally still there was a greater growth of the intraosseous cysts, which destroyed the bone and extended into the soft parts around the vertebrae. Toxic action was not evident around the cysts, but there was an unusually strong inflammatory reaction around necrotic cysts, which suggested that the degeneration products of the cysts had a toxic action. The histopathological changes observed are described in detail and for these the paper itself must be consulted.

The authors think that in most human cases in which infection of the brain occurs, this infection is primary, *i.e.*, the oncosphere is carried directly to the brain, and that this also happened in the first vole described by them; but the infection of the central nervous system of the second vole was secondary by metastasis from cysts in the liver; in many of their experimentally infected mice portions of primary cysts in the liver were detached and formed new cysts at several places in the abdominal cavity. The penetration of the cysts into the vertebral column was unusual and there is no known case in man in which it has occurred. Fischer (*loc. cit.*), however, cites about a dozen cases in which the larval phase of *E. granulosus* first settled in the vertebrae and then gradually grew into the vertebral canal and produced a condition similar to that caused by *E. multilocularis* in one of the voles here described.

G. Lapage

DENES DE NEGRI, ROSITA & LUPPI, A. L'anchilostomiasi rurale e le altre parassitosi intestinali in un comune del Polesine: Lusia (Rovigo). [**Rural Ankylostomiasis and Other Intestinal Parasitic Diseases in a Polesine Commune: Lusia**] *Giorn. di Malattie Infettive e Parassit.* 1957, June, v. 9, No. 6, 303-9, 6 figs. [30 refs.]

The commune of Lusia is in the Po delta a few kilometres west of Rovigo and this paper deals with the epidemiology of infection by certain intestinal helminths there. The commune is roughly rectangular, nearly 4,500 acres in extent, and had a population at the last census of 4,534. It is low-lying, the soil is sandy and the climatic conditions for a great

part of the year very suitable for the survival of ankylostome larvae. The work is almost exclusively agricultural—chiefly horticulture—the water supply most inadequate, arrangements for the disposal of excreta so unsatisfactory as to be virtually absent, and in addition the vegetables are fertilized by a combination of chemicals, animal and human faeces. It is easy to see therefore that ankylostomiasis once introduced is able to flourish.

With the helpful cooperation of the inhabitants, to which the authors pay tribute, investigations were carried out from May to October 1954 and from February to October 1955 on specimens of faeces from 707 males and 722 females of all age-groups from one part of the commune; the specimens were then examined by Ritchie's method.

161 males and 156 females were found positive for ankylostomes, the highest infection rate being in the 16–30 age-group in both sexes and, as might be expected, by far the highest rate was in the market gardeners, 50% of whom were infected.

In addition, *Trichuris* infection was also very high, especially in females; it was present in 80% of females harbouring worms. *Ascaris* was also fairly common.

The authors hope that ankylostomiasis will be scheduled as an occupational disease of agricultural workers, but they note particularly that the majority of those found to be positive were in quite good health.

[As this was an entirely epidemiological investigation no blood counts were made. It would, however, be interesting to have subsequently a haematological comparison to set against the rough clinical estimation of the condition of the patients given above.] W. K. Dunscombe

BEECKMANS, G. Un cas d'anémie grave chronique due à une ankylostomiase rebelle. [**A Case of Severe Anaemia due to Persistent Ankylostomiasis**] *Ann. Soc. Belge de Méd. Trop.* 1957, Feb. 28, v. 37, No. 1, 123–6.

The English summary appended to the paper is as follows:—

“Relation of a case of a 11 months old child suffering from acute anaemia associated with ancylostomiasis. The anaemia resisted to transfusions, intramuscular iron and chenopodium oil, but yielded to tetrachlorethylene followed by antimalarial treatment and intramuscular iron.”

SADUN, E. H., ALLAIN, Dorothy & HEIMLICH, R. **Quantitative Determination of *Ascaris* Eggs in Clear Suspensions by Photonephelometry.** *Exper. Parasit.* New York. 1957, May, v. 6, No. 3, 271–9, 3 figs.

The standardization of suspensions of protozoa and helminths for experimental use is laborious and variable, and therefore the photometric methods used in estimating the concentration of bacterial suspensions were applied to suspensions of the eggs of *Ascaris lumbricoides* var. *suis*.

Clear suspensions were made of eggs obtained from the uterus of adult female worms. [The original should be consulted for details of the technical methods and for the results and their statistical examination.]

The results show that estimates of the concentration of the eggs in clear suspensions are less variable and are done more rapidly by photometric methods than by direct egg counts.

W. E. Kershaw

GREEN, N. M. **Protease Inhibitors from *Ascaris lumbricoides*.** *Biochem. J.* 1957, July, v. 66, No. 3, 416-19, 2 figs. [12 refs.]

LIANG, Shu-Fang, WANG, Hsüeh-Ch'iao, WANG, Ts'ui-Hsiang & LIU, Mei-Fang. **Parasitic Invasion of the Biliary Tract. A Report of 140 Surgically Treated Cases.** *Chinese Med. J. Peking.* 1957, May, v. 75, No. 5, 418-20.

Routine stool examinations from 80,763 patients in 8 hospitals in Shanghai revealed 19,218 (23·8%) positive for *Ascaris ova* and 19 (0·023%) for *Clonorchis sinensis*. Study of 1,685 biliary tract operations in 11 hospitals showed that in 138 cases *Ascaris* was involved while in only 2 was *Clonorchis* present. The authors report on these 140 cases.

The manifestations of *Clonorchis* were largely those of cholangio-hepatitis. In one of the patients 114 flukes were removed from the biliary tract: in the other, who died later, ova were found in the bile aspirated at operation.

The 138 patients with *Ascaris* were mostly young females, but their ages ranged from 3 to 60 years. Clinically there were 2 groups: the first showed symptoms suggestive of an acute abdomen, but fever and jaundice were absent in early cases: in the second group there was a history of biliary trouble, the pain was less severe, but fever and jaundice were commoner. Tenderness in the right upper abdomen or in the substernal region was the most important sign. In 13 patients tenderness occurred in both quadrants and 7 of these had acute pancreatitis. There was leucocytosis up to 20,000 per cmm. and in 80% *Ascaris* ova were found in the stool. Demonstration of ova in bile aspirated from the common bile duct at the time of operation was often helpful and is recommended as a routine.

Treatment of *Clonorchis* infection consisted of removal of parasites, stones, and the gall-bladder, dilatation of the sphincter of Oddi and drainage of the common bile duct.

In early *Ascaris* infection, the parasites were removed from the incised common bile duct, the gall-bladder was evacuated and the common bile duct drained; in 11 very early cases, the last step was omitted, with good results. Where the gall-bladder was inflamed, cholecystectomy and drainage of the common bile duct were carried out. Experience of 9 recurrences after operation indicated the need for early anthelmintic

treatment in biliary ascariasis and it was found best to introduce the drug into intestinal tract at the time of operation. The authors eventually used 2% saturated solution of santonin in alcohol. A "single dose" [amount not stated] diluted with 50 to 100 cc. normal saline as a fine suspension is introduced through a rubber catheter into the duodenum or even into the common bile duct at the time of operation. The ascarids thus lose their activity, are carried downwards by peristalsis and eventually passed in the faeces. With this treatment the authors experienced no more postoperative recurrences.

In the series of 140 surgical cases, there were 4 deaths, 1 of a patient with clonorchiasis and 3 of patients with ascariasis. The principal post-operative complications were cholaemia and hepatic failure where cholangiohepatitis was present.

[See also this *Bulletin*, 1957, v. 54, 723, 724.]

H. J. O'D. Burke-Gaffney

SOUTH PACIFIC COMMISSION. Noumea, New Caledonia. **Report of an Investigation on Filariasis in the Berau Region (Inanwatan District, North-West New Guinea)** [DE ROOK, H.]. *Technical Paper No. 105*. 1957, May, v + 19 mimeographed pp., 3 maps & 2 figs. [19 refs.]

The Berau region of New Guinea lies between the Metamani river on the west and the Sebjar on the east, and forms part of the administrative district of Inanwatan. There is a narrow strip along the north coast of the McCleure Gulf and a water-logged swamp, 20 miles in length by 9 miles in width to the north of this. 6 villages are scattered over this large area and elephantiasis is common in them.

The entire populations of two villages, excluding children under one year, were examined. Blood samples were taken at night between 8.0 and 10.30 p.m. 857 persons were examined in Negeri Besar and 322 in Kasueri villages. The microfilaria rate was high in both, being 25.7 and 29.1 respectively. The type was the nocturnal periodic form of *Wuchereria bancrofti*. Observations by DE GROOT on 4 carriers from Negeri Besar exhibited characteristic nocturnal periodicity. The average count was highest at midnight and the 6 a.m. count was high in comparison with the 6 p.m. count [as was also recorded by BURCH and GREENVILLE (this *Bulletin*, 1955, v. 52, 807) in Liberia.

In these 2 villages 114 cases of gross manifestations of filarial disease were recorded. Classification of these showed elephantiasis of the leg (60) to be the most common, followed by hydrocele. No cases of elephantiasis of the arm, mammae or penis were recorded, and the incidence of microfilariae in persons with filarial disease was not different from that in persons without. In those with hydrocele and fibrosis of the testis the incidence was much higher than in those with elephantiasis of the leg or scrotum. The incidence of filarial disease was equal in males and females, but the microfilaria rate (23.8) was slightly higher in the former than in the latter (17.8).

In both villages the infection rate, following the rule, increased progressively with age. The vectors are *Culex annulirostris*, *Mansonioides uniformis* and *Culex bitaeniorhynchus*. Development also took place in *Aedes kochi* and *Mansonioides papuensis* in a limited trial. The parasite completed its development in each of them, reaching the infective stage in 12½ days. Natural infection rates of 20–30% were recorded in the 3 first-named species which are, moreover, domestic and anthropophilic and form the bulk of mosquitoes found in houses. *Culex annulirostris* and *C. bitaeniorhynchus* were found breeding extensively in the marsh around and close to the habitations.

So far *Anopheles punctulatus farauti* has been regarded as the major vector of filariasis in New Guinea, but in the present study no anophelines were found in the area.

Diethylcarbamazine (Hetrazan) prophylaxis, though promising good long-term results, could not be applied on account of local difficulties. Under the prevailing conditions spraying with residual insecticides promises good results in this form of filariasis. *Philip Manson-Bahr*

DISSANAIKE, A. S., DISSANAIKE, G. A., NILES, W. J. & SURENDRANATHAN, R. **Further Studies on Radioactive Mosquitoes and Filarial Larvae using Autoradiographic Technique.** *Exper. Parasit.* New York. 1957, May, v. 6, No. 3, 261–70, 1 fig. & 2 pls.

Infective larvae of *Wuchereria bancrofti* and *Setaria digitata* with high β activities have been obtained by allowing the microfilariae to develop after ingestion in *Culex fatigans* and *Armigeres obturbans*, the adult forms of which had been made radio-active by transferring the 2nd and 3rd stage mosquito larvae to baths containing ^{32}P . Oviposition did not occur in the mosquitoes, but the development of the filarial larvae was not seriously affected by the large radiation dosage. The distribution of ^{32}P in the mosquitoes, pupae and infective filarial larvae was studied by autoradiography. The infective filarial larvae had counting rates high enough for them to be traced in the definitive host tissue by dissecting the tissues at the site of inoculation, and then by detecting the larvae by using a β counter or by autoradiography.

[The original should be consulted for the technical details.]

W. E. Kershaw

BRUIJNING, C. F. A. **Notes on the Common Species of *Culicoides* (Diptera: Ceratopogonidae) from Surinam in relation to ozzardi-Filariasis.** *Documenta Med. Geograph. et Trop.* Amsterdam. 1957, June, v. 9, No. 2, 169–72. [19 refs.]

“(1) Three species of *Culicoides* are reported from Surinam, *C. guttatus* (Coquillett), *C. paraensis* (Goeldi) and *C. debilipalpis* Lutz.

“(2) *C. guttatus* is very common in the endemic ozzardi-filariasis areas.

" (3) Filarial larvae were observed in the proboscis of two specimens of *C. guttatus* captured in the Amerindian village of Matta. Many inhabitants of this village have *ozzardi*-microfilariae in their blood.

" (4) The *ozzardi*-filariasis in Surinam is confined to the Amerindians.

" (5) The failure of *ozzardi*-filariasis to spread in the other ethnic groups of the population may be explained (a) by the limited flight range of *C. guttatus* and (b) by the isolation of the Amerindian villages."

HSIEH, H. C. & CHUANG, C. H. **A Note on the Periodic Appearance of Microfilaria of *Dirofilaria immitis* Leidy in the Peripheral Blood of an Indigenous Dog in Taiwan (Formosa).** *J. Formosan Med. Ass.* 1956, Oct., v. 55, No. 10, 502-4.

D'HAUSSY, R., PFISTER, R., RIT, J. M. & BRETEAU, G. Note sur les relations de l'onchocercose et de la syphilis au Soudan. [**Relations between Syphilis and Onchocerciasis in the French Sudan**] *Bull. Soc. Path. Exot.* 1957, Mar.-Apr., v. 50, No. 2, 314-21.

The authors have investigated the possible inter-relationship of onchocerciasis and syphilis in the aetiology of lesions of the anterior and posterior segments of the eye in a group of villages near Bamako, French Sudan; these are sited on the banks of the river Baoulé, a tributary of the Niger.

They set out to determine (a) whether onchocerciasis gives false positive sero-reactions for syphilis, and (b) whether syphilis influences the development of onchocerciasis, especially the posterior segmental lesions in the eye. They remark that filarial diseases were held to be a cause of false positive sero-reactions for syphilis in years gone by, when antigens were less specific than they are today.

Onchocerciasis was diagnosed by the finding of typical nodes, by the recognition of microfilariae swimming in the anterior chamber of the eye or by their demonstration in smears or biopsy specimens of the skin. The sero-diagnosis of syphilis was based on the results given by three different tests, the Kolmer, the Kline and the VDRL reactions. In some instances sera were sent to Paris where a treponemal immobilization test was carried out.

The area chosen was one in which both onchocerciasis and a treponemal disease were intensely endemic. The overall incidence of onchocerciasis was 73%: 43% of children were infected and almost all the adults (94%). The treponemal investigation showed that of the whole population, 64% were sero-positive, 28% sero-negative, while in 7% the results were equivocal. Positive sero-reactions were attributed to syphilis rather than to yaws, since the villages were situated in dry savannah country, interstitial keratitis and deafness were found and gummatous skin lesions were encountered. [The last does not constitute a distinction from yaws.]

The findings may thus be summarized:—

(a) In patients showing lesions typical of onchocerciasis in the anterior segment, the incidence of positive and negative sero-reactors was the same as that in the population as a whole.

(b) With regard to lesions in the posterior segment, among patients with choroidoretinitis with or without associated optic atrophy, 17 out of 21 (80%) were sero-positive: for so small a number this figure did not seem to differ significantly from the overall incidence of sero-positivity. Primary optic atrophy was found in 5 of the 67 onchocercal subjects who showed posterior segmental lesions: all had positive sero-reactions. Patients showing colloid bodies or *drüsen* were generally sero-negative, but this lesion was not considered to be related to onchocerciasis either.

The authors' final conclusions are that by the use of the three tests in combination a positive reaction is a true indication of an antecedent treponemal infection, and that there exists no relationship between treponematosis—syphilis in this instance—and the development of the eye lesions of onchocerciasis.

[In the majority of subjects who showed posterior segmental lesions of the eyes, onchocercal and syphilitic infections undoubtedly co-existed. The abstractor doubts whether, save in rare instances, any differentiation could be made.]

J. H. Walters

VAN THIEL, P. H. **The Infestation of the Population of the Netherlands with *Enterobius (Oxyuris) vermicularis*.** *Ztschr. f. Tropenmed. u. Parasit.* Stuttgart. 1957, v. 8, Nos. 1/2, 270–74.

The author refers to earlier studies of enterobiasis in the Netherlands and gives the results of his study of 1,035 Navy recruits, mostly aged 19 or 20 years, who were examined before they had bathed by the pestle method of SCHÜFFNER and SWELLENGREBEL [this *Bulletin*, 1945, v. 42, 922] just before they joined up. Many pestles were used in turn and were repeatedly rinsed in a tank of water and disinfected with lysoform. Before use they were rinsed in water and dried with a clean cloth.

On an average 32.2% of the recruits "appeared to be positive at the first examination". The author thinks that 5 successive examinations would have shown a higher percentage of positives, "say, 50 per cent."

SMALT (*Nederl. Tijdschr. v. Geneesk.*, 1944, v. 88, 240) found that 62.4% of industrial labourers at Amsterdam were positive; and among 19 of the recruits examined by the author, who said they were textile or factory workers, 10 were positive. The recruits, however, included very few factory workers and the author thinks that there are greater chances of aerial infection in factories in which a number of people are working together. He also thinks that, although he found that the number of children in the families of 99 of the recruits did not influence the degree of infection, the family is nevertheless the main source of infection.

The author concludes that the infection is "rather equally" distributed throughout Holland and that statistically significant differences in the incidence are shown only by the provinces of Brabant and North and South Holland, and that this may be related to poorer hygiene or to a larger number of children in these provinces.

Recruits rarely complained of the infection.

G. Lapage

SYMMERS, W. St. C. **Two Cases of Eosinophilic Prostatitis due to Metazoan Infestation (with *Oxyuris vermicularis*, and with a Larva of *Linguatula serrata*).** *J. Path. & Bact.* 1957, Apr., v. 73, No. 2, 549-55, 3 figs. on pl. [20 refs.]

The author briefly refers to the rarity of metazoan parasites in the prostate and quotes literature on the occurrence of schistosomiasis and *Echinococcus* cysts there. He records 2 cases of granulomatous prostatitis caused respectively by *Enterobius vermicularis* and the nymph of the tongue-worm of the dog, *Linguatula serrata*. The eosinophilic infiltration of the prostate associated with these two infections must be differentiated from the eosinophilic prostatitis described in asthmatic patients by STEWART *et al.* (*J. Path. & Bact.*, 1954, v. 67, 423), by HARRISON and NEANDER (*J. Urology*, 1954, v. 72, 1218) and by NICKEY and MONTGOMERY (*ibid.*, 1956, v. 75, 730); and further from "non-specific diffuse granulomatous prostatitis" developing in association with retention of prostatic secretion and its escape into the tissues (see Symmers, *Arch. Pathology*, 1950, v. 50, 475).

The first patient, a medical man aged 46, had, 2 weeks before admission into hospital, difficulty of micturition with acute perineal pain. He reduced his fluid intake and the faeces then hardened and he had pain on defaecation. He had chronic eczema of the scrotum perineal region and adjacent thighs, and his wife and 3 children also had this. The prostate was moderately enlarged and the bladder reached nearly to the umbilicus. The urine was normal. Prostatectomy revealed the presence of *Enterobius*. The faeces contained innumerable eggs and very large numbers of adult worms, and adhesive swabs showed many eggs on the perianal skin and skin of the thighs. The patient's wife and children were also infected and eggs were found in the dust from bedding and bedroom. Anthelmintic treatment controlled the infection in them all. The prostate showed an "oxyuris" granuloma with a necrotic core, mostly composed of degenerating eosinophils and worm eggs, surrounded by granulomatous tissue containing many eosinophils. Eosinophils were also numerous elsewhere in the stroma.

The second patient, a man aged 84, had had mild symptoms of prostatic enlargement for 15 years, but was in good health. He was a breeder of dogs. He developed acute retention of urine, easily overcome by catheterization, but urination was then painful and more frequent, with pain after it. The prostate was moderately enlarged, the urine sterile.

Perurethral resection was done and for 2 years after this there were no symptoms. Before the resection there was a blood eosinophilia (8% of 8,000 white cells per cmm.) and 10 days after it the count was 2% of 6,500 white cells per cmm. Sections of the 9 gm. of prostate removed showed simple myo-fibro-epithelial prostatic hyperplasia, with widespread eosinophilic infiltration of the prostate, and an encysted nymph of *Linguatula serrata*, of which good photographs are given.

The author thinks that the *Enterobius* entered by the urethra, although there is no indisputable record of its entry thus. Prostatic granuloma caused by *Enterobius* has not previously been described, but the author refers to literature on granulomata caused by this worm in the female genital organs, the intestine, the omentum, spleen, kidney, lungs and breast. In the second patient the prostate was doubtless entered by chance. Larvae of *Linguatula serrata* have been most often found in the mesenteric lymph nodes, liver, lung and kidney; infection of the prostate by them has not been previously recorded. The anatomy, life history and incidence of *L. serrata* are discussed.

G. Lapage

SADUN, E. H. & ALLAIN, D. S. **A Rapid Slide Hemagglutination Test for the Detection of Antibodies to *Trichinella spiralis*.** [Research Notes.] *J. Parasitology*. 1957, June, v. 43, No. 3, 383.

“These preliminary experiments indicate that antibodies in the sera of trichinosis patients with *Trichinella* infections can be measured in a slide hemagglutination test by adsorbing the antigen onto tanned erythrocytes. Since no attempts have been made to evaluate this test and to compare it with the standard hemagglutination test, no knowledge is yet available as to the sensitivity and specificity of this test. It should be pointed out, however, that this test offers the great advantages of being performed in a very short time, of being much easier to read, and of requiring very minute amounts of antigens and antisera.”

DEFICIENCY DISEASES

RAOULT, A. L'éducation alimentaire en Afrique Occidentale Française. [Nutrition Education in French West Africa] *Méd. Afrique Noire*. Dakar. 1957, May 1-15, v. 4, No. 9, 175-81.

This is a long essay dealing with the difficulties and problems of health education in undeveloped countries. A very comprehensive programme of the Public Health Services is described and clearly the French are very alive to the importance of health education in Africa, especially

among the illiterate. The author is optimistic and considers that a spontaneous desire for education is arising in Africa which will help to raise the levels of living.

R. Passmore

CHANDLER, A. C. **Interrelations between Nutrition and Infectious Disease in the Tropics. Presidential Address.** *Amer. J. Trop. Med. & Hyg.* 1957, Mar., v, 6, No. 2, 195-208. [Numerous refs.]

This is a scholarly address packed with information and common sense and written with charm. The first half is concerned with the complex factors that determine the competition between host and parasite for a limited supply of nutrients. This account is fully documented. In clinical practice the patient will not be restored to full health unless attention is paid both to the diet and to all the infectious agents. The second half is a plea for foreign aid programmes. Both moral responsibility and economic circumstance combine so that "we cannot . . . ignore the welfare, particularly the health, of the under-privileged countries . . .".

[It is impossible to abstract this excellent address adequately and all interested in the fundamentals of tropical medicine are strongly advised to read it.]

R. Passmore

GOPALAN, C. **Malnutrition among Infants and Young Children in India.** *J. Trop. Pediatrics.* London. 1957, June, v, 3, No. 1, 3-12. [11 refs.]

This is a general survey which sets out mortality rates, the expectation of life, infant mortality rates, nutritional status of pregnant women, infants and young children and heights and weights of children under 5 years. The data are taken mostly from surveys in South India. The infant mortality rate in Madras City was 136 in 1954. This high figure epitomizes the rest of the data and shows what a formidable task lies before the health services in India.

R. Passmore

VOORS, A. W. **The Use of Dental Age in Studies of Nutrition in Children.** *Documenta Med. Geograph. et Trop.* Amsterdam. 1957, June, v, 9, No. 2, 137-48, 2 figs. [32 refs.]

In assessing nutritional status, as part of a Public Health programme, it is often important to have accurate knowledge of the ages of children. In many underdeveloped countries neither the children nor their parents have this knowledge. This paper reviews the possibility of using the eruption of both the deciduous and permanent teeth as a measure of skeletal age. The author also recorded the dental state of 208 indigenous children in Netherlands New Guinea, for each of whom there was an

accurate record of age in missionary registers of baptism. It is concluded that the determination of dental development is a useful method for determining age in the assessment of nutritional status.

[One can agree with this conclusion of the author's, but a *caveat* must be added. The method can only be used if the observers are skilful in identifying teeth and if the numbers of children are sufficiently large to allow statistical treatment. Provided these factors are satisfied, this may prove to be an important addition to the techniques of nutritional survey in some countries.]

R. Passmore

YAP-KIE-TIONG. A Comparative Study of the Diets, and Results of some Blood Analyses, of Children living in Different Environments in Jogjakarta (Central Java). *Brit. J. Nutrition.* 1957, v. 11, No. 2, 158-61.

Children living in a poor district in Jogjakarta were found to consume an insufficient diet based on rice and tubers. The diets were lacking in calories, proteins, calcium and iron and the principal vitamins. Blood levels of albumin, haemoglobin, calcium, vitamin A and carotene were low. A group of children of doctors in Jogjakarta were found to consume a good diet and to have normal levels of blood chemistry. *R. Passmore*

HUENEMANN, Ruth L., BRUCH T., H. A. & SCHOLES, R. T. A Dietary Survey in the Santa Cruz Area of Bolivia. *Amer. J. Trop. Med. & Hyg.* 1957, Jan., v. 6, No. 1, 21-31.

This paper records a dietary survey of 20 Mestizo families and 12 post-weaning children in the Santa Cruz area of Bolivia. Intakes of calcium, thiamine, riboflavin and vitamin A were generally low. Intakes of calories, protein, iron and ascorbic acid were often unsatisfactory. Rice, yuca, refined bread, coffee, sugar and varying amounts of meat were the major items of diet. A programme of home growing of food and possible changes in food preparation and buying practices are suggested as ways of improving the diets.

R. Passmore

FAIN, A. & FALAISE, A. Calculose vésicale et avitaminose A chez les enfants au Ruanda-Urundi. [Vesical Calculus and Vitamin A Deficiency in Children in Ruanda-Urundi] *Ann. Soc. Belge de Méd. Trop.* 1957, Feb. 28, v. 37, No. 1, 135-7, 1 fig. on pl.

The English summary appended to the paper is as follows:—

“It is quite clear that urinary lithiasis appears more frequently among the natives of Ruanda-Urundi than among those of Belgian Congo; most of the patients who have been observed by the authors the last few years,

are children, always male children from 6 to 11 years old and bearers of sometimes very voluminous vesical stones. The vesical lithiasis causes among these young boys a characteristically clinical syndrome which is accompanied, in a constant manner, by symptoms more or less evident of Avitaminosis A, and it might be well to consider what part this deficiency takes in the formation of these voluminous stones."

GLASER, E. M. & LIVETT, B. H. **Effect of Vitamin-B Complex on Healthy People in a Warm Climate.** *Brit. Med. J.* 1957, June 8, 1331-2. [18 refs.]

Tablets, each containing 8 components of the vitamin-B complex, were given daily to each of 79 apparently healthy medical students in Singapore for 6 weeks. Dummy tablets were also given for a period of 8 weeks. The vitamins produced no improvement of the subjective sense of well-being and no decline in the incidence of minor illnesses in the subjects.

R. Passmore

BUSSON, F., TOURY, J., GUTH, P. & ROLLAND, M. Composition en acides aminés d'un tourteau d'arachide. [**Amino-Acid Content of Ground-Nut Cake**] *Méd. Trop.* Marseilles. 1957, May-June, v. 17, No. 3, 428-36, 4 figs. [18 refs.]

BUSSON, F., PERISSE, J., ROLLAND, M. & MEAL, H. Sur la composition des protides des graines de Baobab. [**The Protein Content of Baobab Seeds**] *Méd. Trop.* Marseilles. 1957, May-June, v. 17, No. 3, 437-40, 2 figs.

WATERLOW, J. C. & BRAS, G. **Nutritional Liver Damage in Man.** *Brit. Med. Bull.* 1957, May, v. 13, No. 2, 107-12. [Numerous refs.]

This is a concise review of modern ideas of the role of nutrition in the aetiology of diseases of the liver. Atrophy occurs as a result of simple starvation. In malnourished infants there is a marked reduction of both the total weight of the liver and its protein content. The fatty liver in kwashiorkor is almost certainly attributable to protein deficiency.

There are various forms of cirrhosis of the liver which are much commoner in the tropics than in Europe and North America. These include portal cirrhosis, veno-occlusive disease and childhood cirrhosis in India. There is no strong evidence that any of these forms of cirrhosis are directly attributable to a dietary cause. In particular in no single instance has cirrhosis been demonstrated to have developed in the fatty liver of kwashiorkor. However, much evidence has accumulated in the

last 10 years consistent with the view that a deficient diet, consumed over several years, predisposes to injury by toxins, parasites and viruses. A theory of the dual origin of cirrhosis would reconcile many discrepancies, particularly in the epidemiology of the disease. *R. Passmore*

WATERLOW, J. C. & SCRIMSHAW, N. S. The Concept of Kwashiorkor from a Public Health Point of View. *Bull. World Health Organization*. Geneva. 1957, v. 16, No. 2, 458-64. [25 refs.]

The diagnosis of kwashiorkor in a child sufficiently ill to be admitted to hospital seldom presents difficulties. But from the public health point of view it is the number of children in a community who are suffering from minor manifestations of the disease that is important. Here diagnosis is difficult. Where is the line to be drawn between health and disease? If statistics and reports from different places are to have any comparable meaning, agreement on acceptable essential criteria for diagnosis is necessary. The authors suggest that it would be of great value if all such reports were to contain a frequency table of the various changes observed. The paper contains a table drawn from reports in 8 parts of the world showing the association of 8 clinical manifestations—growth retardation, psychic changes, oedema, skin lesions, hair changes, hepatomegaly, subcutaneous fat retained, and diarrhoea.

R. Passmore

CARR, W. R. & GELFAND, M. Observations on Diet, Certain Vital Statistics and Biochemistry in Kwashiorkor Cases treated in Salisbury. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1957, May, v. 51, No. 3, 229-37, 2 figs. [12 refs.]

Figures are given for monthly admission rates of patients with kwashiorkor to Salisbury African Hospital, and show a big increase in the "hungry months"—January to March.

Serum protein measurements were made on patients during treatment. Levels of albumin recovered rose only slowly, but α_2 and β globulin levels rose rapidly. There was an average increase of α_1 globulin levels to 0.43 gm./100 ml.; the normal figure found in healthy African children being 0.35 gm./100 ml. From the table of results there also appears to have been a substantial increase in γ globulin levels, though the authors report no change in the discussion and summary. *R. Passmore*

POLITZER, W. M. & WAYBURN, S. Serum Electrolytes and Proteins in Kwashiorkor. *Brit. J. Nutrition*. 1957, v. 11, No. 2, 105-11, 1 fig.

The serum sodium and potassium levels were measured in 63 children with kwashiorkor. There was no correlation between the degree of

oedema and the level of serum sodium. Serum potassium levels were reduced in patients with diarrhoea and very low (below 3.0 m-equiv. per litre) in 4 of the 11 fatal cases.

R. Passmore

SCHWARTZ, Ruth & DEAN, R. F. A. **The Serum Lipids in Kwashiorkor.**

I. Neutral Fat, Phospholipids and Cholesterol. *J. Trop. Pediatrics.*

London. 1957, June, v. 3, No. 1, 23-31, 2 figs. [23 refs.]

Values for serum lipids in 20 African children with kwashiorkor were low on admission, but rose during treatment. For 14 children the mean value for total lipids rose from 532 to a maximum of 969 mgm./100 ml. serum. Corresponding changes for phospholipids were 145 to 206, for neutral fats 241 to 486, for total cholesterol 105 to 190 and for free cholesterol 49 to 63. After the rise, which usually reached a maximum within 10 days there was a gradual fall, but not to as low a level as before treatment.

Changes of the same order occurred both on a fat-free diet and a diet containing cotton seed oil (50 gm. daily). It is suggested that the rise in serum lipids results from the release of tissue fats, probably especially liver fat. Failure to mobilize liver fat may be a significant feature of kwashiorkor.

R. Passmore

BADR EL-DIN, M. K. & ABOUL WAFI, M. H. **Pancreatic Activity in Normal and Malnourished Egyptian Infants.** *J. Trop. Pediatrics.*

London. 1957, June, v. 3, No. 1, 17-22.

Pancreatic juices were obtained by duodenal intubation in 19 normal infants, in 9 with kwashiorkor and 4 with marasmus. In these diseases the juice was scanty and contained excess mucin. Tryptic activity was very low. Amylase content was reduced or sometimes normal in kwashiorkor, but normal in marasmus. The tryptic activity appeared to diminish before the classical signs of kwashiorkor developed.

R. Passmore

SCRIMSHAW, N. S., BÉHAR, M., ARROYAVE, G., TEJADA, C. & VITERI, F. **Kwashiorkor in Children and its Response to Protein Therapy.**

[Report to the Council on Foods and Nutrition (WHITE, P. L., Secretary).] *J. Amer. Med. Ass.* 1957, June 1, v. 164, No. 5, 555-61, 11 figs. [Numerous refs.]

This is an excellent summary of the clinical, pathological and biochemical findings in kwashiorkor. The Council on Foods and Nutrition of the American Medical Association are making the paper available in a monograph form and this should be a useful contribution to medical education in America. Regular readers of this *Bulletin*, however, are not likely to find anything new in the paper.

R. Passmore

PAQUE, C. Hydropolydipsie ou maladie de l'eau. Un syndrome complexe de l'enfance marocaine. Son importance dans l'étiologie des syndromes de polycarence de l'enfance (Malnutrition, Kwashiorkor). [**Hydropolydipsia or the Water Malady. A Complex Syndrome of Moroccan Infants. Its importance in the Aetiology of the Syndromes of Multiple Deficiency in Infancy (Malnutrition, Kwashiorkor)**] *Maroc Méd.* 1957, Apr., v. 36, No. 383, 382-90, 3 figs. [12 refs.]

A condition is described in Moroccan infants in which the child loses all appetite for food and takes only water in large quantities by mouth. A number of factors are responsible. These include a poor diet after weaning and the hot climate in summer, which causes excessive water losses in the sweat. The child becomes thirsty and the mother repeatedly gives the child water. Maternal ignorance and a psychological desire to comfort the child by giving something, no matter what, are in part responsible.

The author gives brief clinical notes of 29 patients. Total anorexia was the chief finding; oedema was present in most and intercurrent infections were common, as were also signs of dietary deficiency diseases.

R. Passmore

HAEMATOLOGY

TREDRE, R. F. **Iron-Deficiency Anaemia. Ross Institute Industrial Advisory Committee: Information and Advisory Service. London School of Hygiene and Tropical Medicine.** 1957, Feb., Bull. No. 11, 23 pp., 1 diagram. [13 refs.]

This is an excellent monograph on what is a very important subject, causing as it does a great amount of morbidity throughout the tropics. After outlining the characteristics, constituents and substances needed for production of red blood cells, Dr. Tredre discusses the various causes of iron deficiency anaemia and succinctly reviews the importance played by diet, faulty metabolism of iron and parasitic infections. Stress is laid on the basic importance of protein in the diet in the prevention of anaemia. In the second section of the monograph the problem presented by the disease is elaborated under the heads of protein malnutrition and metabolism of iron, including physiological requirements, excretion and absorption. There follows a section on treatment in which it is emphasized that there is a tendency for those treated to regress and that treatment may be required for weeks before improvement is obtained. The value of coincident administration of protein supplements is emphasized.

The third section consists of a final comment and a note on what can be done to prevent the disease on a community basis.

The monograph contains a concise synopsis of much recent work on the subject and Dr. Tredre and the Ross Institute are to be commended on producing it, for focussing attention upon an important and often overlooked subject, for the sound practical advice which is given and for the balanced appraisal of the problem.

A. W. Woodruff

WOODRUFF, A. W. & SCHOFIELD, F. D. **Haemoglobin Values among Gambians.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1957, May, v. 51, No. 3, 217-20.

The haemoglobin levels were determined in villages in the Gambia in 100 men aged 17-45 years, and in 101 non-pregnant women within the same age-group. The means were 11.76 and 10.12 gm. respectively. The mean haemoglobin level in 87 pregnant women was 9.09 gm. When the people with a haemoglobin level below 8 gm. were examined for ankylostomiasis, malaria and trypanosomiasis, it was seen that the correlation between anaemia and ankylostomiasis was more close than that between anaemia and overt malaria. Of 31 such severely anaemic patients only 5 had malaria parasites in their blood, but 25 had hookworm ova in their stools. Though malnutrition, liver damage and malaria may all be contributory factors in bringing about the universally low haemoglobin level in the Gambia [this *Bulletin*, 1955, v. 52, 395], infection with hookworms seems to be the most important cause. H. Lehmann

SCHOFIELD, F. D. **Aspects of Nutritional Anaemia in Pregnancy in Gambia.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1957, May, v. 51, No. 3, 221-8. [30 refs.]

The author has examined in the Gambia 11 women with anaemia of pregnancy in whom the cause of the anaemia was not malaria, infection with hookworms or iron deficiency. Many pregnant women with anaemia due to these causes were also seen and they responded to the appropriate treatment. Thus the 11 cases described in this paper are not representative of all, or even the majority, of anaemias of pregnancy in the Gambia. 8 of the women had a high mean corpuscular red cell volume and there was a high reticulocyte count in 6 of them. The high reticulocyte levels suggested that there was increased haemolysis. After delivery the reticulocyte counts fell and remained low for more than two weeks. 2 women had normocytic and 1 had microcytic anaemia. The bone-marrow of the pregnant women showed a picture transitional between that of megaloblasts and normoblasts. There was no response of the anaemia to added dietary protein but there was spontaneous remission after delivery.

The author suggests that in the 8 patients with macrocytic anaemia there were two factors: a haemolytic factor which disappears directly on delivery and in the production of which past malarial infection can be

suspected of playing a part, and another causing a failure of utilization of haemopoietic substances during pregnancy, which disappears about a week after delivery.

H. Lehmann

Theron, J. J. & Meyer, B. J. **The Influence of Pyridoxine on Iron Absorption in the Pregnant Bantu.** *South African J. Lab. & Clin. Med.* 1956, Dec., v. 2, No. 4, 327-35, 1 fig. [30 refs.]

It is now well-known that siderosis is frequently encountered in the organs and tissues of the Bantu, and it has been reported that during pregnancy the haemoglobin of Bantu women does not fall. These findings have been ascribed to their high dietary iron intake consequent upon their cooking food in iron utensils. An alternative cause is that a dietary deficiency might alter iron metabolism and in this connexion the authors' attention has been attracted by work indicating that pyridoxine deficiency may occur in pregnancy and that absorption of iron may then be increased or its excretion be decreased. It was accordingly decided to investigate the influence of pyridoxine on iron metabolism in pregnant Bantu women with relatively high serum iron values.

The fasting serum iron and the haematological indices were determined during the last trimester of pregnancy; to one group of 10 women 1.6 gm. ferrous gluconate was then given orally and further serum iron estimations made 1, 3 and 8 hours later; to a second similar group the same amount of iron was given together with 100 mgm. pyridoxine intravenously administered; to a third group of 8 patients 10 mgm. elemental iron was administered intravenously in the saccharated form, and to a fourth group, also of 8 patients, the same amount of iron with 100 mgm. pyridoxine was administered intravenously. In both third and fourth groups serum iron estimations were made before, 5 minutes after and 120 minutes after the administration of iron or of iron and pyridoxine.

Fasting serum iron levels of approximately 100 μ gm.% were found in patients in the first two groups. In those to whom iron was administered by mouth this figure rose in 3 hours to 260 μ gm.% and dropped to 180 at the end of 8 hours. A rise after 3 hours to a mean of only 140 μ gm.% was found after the administration of iron orally with 100 mgm. pyridoxine intravenously, and this value was unchanged at the end of 8 hours. The injection of iron to patients in group 3 raised the serum iron from a mean of 126 μ gm.% to a mean of 217 μ gm.% after 5 minutes, this increase representing the unsaturated iron-binding capacity of the serum. The decrease from the value 5 minutes after the injection to that found 120 minutes after the injection represents the tissue iron uptake and this averaged 35 μ gm.% in the third group and 65 μ gm.% in the fourth group in which pyridoxine was administered intravenously along with the iron. From this it seems that pyridoxine increases the tissue uptake of intravenously administered iron, but larger groups of patients would have to be studied before this can be regarded as proved.

The absorption of iron, it is stated, is believed to be normally controlled by a "mucosal block" in the intestinal wall. This block is probably relative and is dependent on diet. It appears to be broken down by lack of pyridoxine and by large amounts of iron in the diet especially if at the same time the phosphate content of the diet is low. Protein deficiency also appears to render the mucosal block ineffective.

[This work is important in that it may explain many anomalous findings relating to siderosis and iron deficiency anaemia.]

A. W. Woodruff

SILVESTRONI, E. & BIANCO, I. Il problema del morbo di Cooley e delle anemie microcitemiche in Italia. Nota II.—Aspetti epidemiologici. [**Cooley's Disease and Microcytic Anaemias in Italy. Epidemiological Aspects**] *Igiene e San. Pubblica*. Rome. 1957, Mar.—Apr., v. 13, Nos. 3/4, 159–68, 2 figs. [36 refs.] English summary.

Extensive investigations involving more than 60,000 persons in Italy have shown that thalassaemia is prevalent in Sicily and also even more so in the Po delta, round Ferrara and Rovigo.

In Sicily the condition is found mainly in the coastal regions, the central mountainous area for the most part having a much lower incidence. The place with the highest proportion was Ragusa (S. Sicily) where out of 132 persons examined 17 had microcytaemia. In the Po delta, where persons from 34 different places were examined, the incidence was even higher. Out of the 34 areas, 13 showed an incidence of 10%–15%, and 10 more than 15%. In 1 place, Mesola, nearly 20% out of more than 1,000 persons examined were affected.

From the numbers found positive the authors estimate that more than 1 million persons are suffering from the disease in Italy, and they ascribe the peculiar geographical location to the fact that the areas most affected were those most extensively colonized by the Greeks, the incidence in that race being known to be high.

The sickle-cell trait and sickle-cell disease are also briefly discussed. These are most common in Sicily and Calabria but not in the Po delta where sickle-cell disease is rare.

W. K. Dunscombe

CHOREMIS, C. & ZANNOS, L. **Microdrepanocytic Disease in Greece.** *Blood*. 1957, May, v. 12, No. 5, 454–60, 3 figs. & 1 map. [13 refs.]

This paper deals with the study of microdrepanocytic disease in Greece, and with its distribution and frequency as compared with those of sickle-cell anaemia. Sickle-cell disease was found in 57 children aged from 16 months to 15 years. Of these 13 were homozygous for the sickling gene, and 44 proved to be heterozygous for this gene and also for that responsible for thalassaemia. As one might expect most of the

children with true sickle-cell anaemia came from a few foci where in Greece sickling is found at high frequency. The geographical distribution of the children with microdrepanocytic disease, however, was much wider.

H. Lehmann

AKSOY, M. & LEHMANN, H. **Sickle-Cell-Thalassaemia Disease in South Turkey.** *Brit. Med. J.* 1957, Mar. 30, 734-8, 2 figs. [30 refs.]

After stating concisely the method of inheritance of sickle-cell anaemia and thalassaemia, the authors describe the clinical characteristics of the disease resulting from inheritance of both genes. Emphasis is placed on the small size of the red blood cells and the presence among them of target cells. These, if of considerable frequency, are an indication of the presence of the thalassaemia gene but other conditions must first be excluded, and most important are the other haemoglobinopathies and severe cirrhosis of the liver.

In 1955 it was observed that there was a high sickling incidence in the Eti-Turks, a small Arabic-speaking enclave near Mersin, in Southern Turkey. In some instances children suffering from sickle-cell anaemia had only one parent whose blood sickled and investigation of these cases led to the discovery of the thalassaemia gene among them. This gene suppresses the formation of haemoglobin A so that heterozygotes who would otherwise have haemoglobins A and S in their blood may possess only haemoglobin S. Among this community it was further found that the heterozygous possession of a sickling and a thalassaemia gene can express itself either as a severe anaemia closely resembling sickle-cell anaemia or as a mild anaemia, or it can be without symptoms.

Clinical details and the family trees of 5 patients with sickle-cell-thalassaemia disease are then given. An unusual feature was the presence of a normal mean cell volume in all cases and of a mean corpuscular haemoglobin concentration which was significantly lowered in only 2. Nucleated red cells were present in 4 patients and 3 had sickled cells in the peripheral blood. Foetal haemoglobin was absent from 2, present in traces in one and present in significantly increased amounts in 2. All patients had a lowered osmotic fragility of their red blood cells. In addition to the 5 patients, all of whom presented symptoms of varying degrees of severity, 2 persons were found to be heterozygotes for the thalassaemia and sickling genes but to be symptom-free.

[The authors have made an important contribution to this field in drawing attention to the possible suppression of haemoglobin A formation by the thalassaemia gene in heterozygotes possessing the thalassaemia and sickling genes. It is therefore important to remember that the finding of only haemoglobin S in the blood cannot be held to imply that the patient is suffering from homozygous sickle-cell anaemia. Before this diagnosis can be made with certainty thalassaemia must be excluded and genetic studies must be carried out.]

A. W. Woodruff

RAPAPORT, S. I., REILLY, E. B. & CARPENTER, G. **Clinically "Intermediate" Thalassemia due to Hypersplenism complicating Thalassemia Minor: a Case Report illustrating Relief of Anemia by Splenectomy.** *Ann. Intern. Med.* 1957, June, v. 46, No. 6, 1199-1207, 3 figs. [16 refs.]

"A patient is described in whom clinically 'intermediate' thalassemia was due to hypersplenism complicating thalassemia minor. This reason for atypical thalassemia warrants particular attention, for it is remediable. In this patient, splenectomy completely corrected a previously fixed anemia."

MODICA, R. & MARAINI, G. Ricerche sulla presenza della falcemia (Sickle-Cell Trait) in Tripolitania. [**The Sickle-Cell Trait in Tripolitania**] *Arch. Ital. Sci. Med. Trop. e Parassit.* 1957, Apr., v. 38, No. 4, 209-18, 3 figs. & 1 map. [17 refs.]

The English summary appended to the paper is as follows:—

"On examining a cross section of the population of Tripolitania, the presence of the Sickle-Cell Trait was demonstrated.

"All carriers of the trait showed characteristics of the negroid race.

"The percentage of carriers to the total number of subjects examined was 0.8%; when related to subjects with negroid characteristics only, the percentage was 4.2%.

"According to some observations on the behaviour of the phenomenon, factors are suspected to exist which might invalidate the previous percentages.

"An enquiry on a bigger scale is being undertaken at present by means of electrophoresis, which should provide more exact figures."

GARLICK, J. P. & BARNICOT, N. A. **Blood Groups and Haemoglobin Variants in Nigerian (Yoruba) Schoolchildren.** *Ann. Human Genetics.* 1957, June, v. 21, Pt. 4, 420-25. [13 refs.]

The authors examined 317 Yoruba schoolchildren, aged 5-9 years, in Ibadan. They determined the incidence of sickling which was 25% and the incidence of haemoglobin C which was 6%. No example of SS was observed. That this was due to chance was a probability of 1 in 120. It thus seems that the SS children die before the age of 5. There was no difference in the incidence of all species of malaria in sicklers and non-sicklers, being 83% in both, but there was a slight difference in height and weight between sicklers and non-sicklers, the mean height of the sicklers being 1.4 cm. more and their mean weight 0.6 kgm. heavier than those of the non-sicklers.

The frequencies of blood groups ABO, MN, Lutheran and Henshaw were determined.

H. Lehmann

EDINGTON, G. M. & LAING, W. N. **Relationship between Haemoglobins C and S and Malaria in Ghana.** *Brit. Med. J.* 1957, July 20, 143-5.

A decline in the incidence of the haemoglobin C gene exists from North Ghana towards the east, south and west, and in the reverse direction for haemoglobin S. If the genes for haemoglobins A, C, and S are in stable equilibrium, the authors postulate that bearers of the C trait have a greater survival potential than normal persons. They therefore attempted to discover whether there existed some protection against malaria for the C-trait in the north, in the same way as had been shown for the sickle-cell trait in the south [this *Bulletin*, 1956, v. 53, 845].

Inhabitants of 3 villages in N.E. Ghana were examined, providing 1,040 capillary blood samples suitable for examination. Paper electrophoresis was performed, and accordingly the subjects could be divided into genotypes: 726 were AA, 190 AC, 21 CC, 89 AS, 14 SC and none SS. Rates and densities of *P. falciparum* were recorded, and the results correlated with the genotypes. For this purpose the subjects were divided into 3 groups: (i) those with normal (AA) haemoglobin, 726 persons, (ii) types AS and SC, 103 persons, (iii) types AC and CC, 211 persons. Members of the second group showed some evidence of protection against malaria in both the frequency and the density of their infections, especially below the age of 5 years, though not to a significant extent. [However, there were only 19 in this group under 5 years of age.] Gametocyte rates were approximately equal for all groups. No protection against malaria was detectable in the third group. But although the authors consider it unlikely that any protection is enjoyed by carriers of the C-trait, they note that this opinion needs confirmation by an investigation of their actual malarial *mortality* compared with that of normal persons.

A second conclusion drawn from this survey is that its negative result means that the absence of protection for sickle-cell carriers in the north, noted in the previous survey, can be taken at its face value.

The paper includes some autopsy data from Accra that are relevant to the subject. These include the observation that of 10 children who had died of proved cerebral malaria, 9 were of AA, and 1 of AG genotype; and 1 child of AC genotype died from "malaria and bronchopneumonia".

Alan B. Raper

RUCKNAGEL, D. L. **Paper Electrophoretic Survey of Hemoglobins of American Indians.** *J. Lab. & Clin. Med.* 1957, June, v. 49, No. 6, 896-9. [13 refs.]

"Blood samples were collected from approximately 150 American Indians from the plains states and from another 100 Indians originating in the southeastern United States. Of the samples examined by electrophoresis, only 3 cases of sickle-cell trait were found. It is thought that these cases of sickle-cell trait are probably attributable to miscegenation with the American Negro."

LEIKIN, S. L. **The Aplastic Crisis of Sickle-Cell Disease. Occurrence in Several Members of Families within a Short Period of Time.** *J. Dis. Children.* Chicago. 1957, Feb., v. 93, No. 2, 128-39, 6 figs. [13 refs.]

One of the late Dr. SINGER's contributions to the pathology of sickle-cell anaemia was the recognition of aplastic crises. These had been described before in hereditary spherocytic anaemia. The cause of the period of aplasia of the bone-marrow can be a suppression of activity by transfusion of blood, *i.e.*, after a blood transfusion the haemoglobin level becomes normal and the bone-marrow is no longer stimulated to produce red cells. Singer suggested that some of these patients are adapted to a low haemoglobin level at which they manage to exist and that if by a blood transfusion a haemoglobin level is achieved above that to which they are accustomed, the bone-marrow ceases to function until such time as the blood level again falls below that to which the individual patient is adapted.

This paper describes aplastic crises occurring in several members of two different families. Although they seemed to follow blood transfusion in some, in others they occurred before a transfusion was given and the authors stress particularly the possibility that infectious agents might play a part in the causation. A search was made for bacteria or viruses which might have been responsible, but unfortunately no specific organism could be found.

H. Lehmann

ELLIS, J. L. & VAN GOOL, J. Een geval van de homozygote vorm van de hemoglobine-C-ziekte. [**Homozygotous Haemoglobinopathia C**] *Nederl. Tijdschr. v. Geneesk.* 1957, June 29, v. 101, No. 26, 1223-6, 4 figs. [31 refs.]

The English summary appended to the paper is as follows:—

“Description of a case of homozygotous haemoglobinopathia C in a patient born in Surinam (South America). This is probably the first time the disease has been demonstrated in anyone of the negroid population of that country. Other haemoglobinopathies may occur there as a result of immigration from India, Java (Indonesia) and China. A shortened life span of the erythrocytes of this patient was demonstrated with the aid of Cr⁵¹. Several aspects of haemoglobinopathia C are discussed.”

AKSOY, M. & LEHMANN, H. **The First Observation of Sickle-Cell Haemoglobin E Disease.** [Correspondence.] *Nature.* 1957, June 15, v. 179, 1248-9, 2 figs.

Search in a community in southern Turkey known to harbour the genes for haemoglobins S and E was rewarded by finding an Eti-Turk woman of 72 years whose blood contained about 40% haemoglobin E and 60%

haemoglobin S. One of her 4 surviving sons by her second husband (deceased) showed the same haemoglobin constitution, and both he and his mother showed a mild normocytic anaemia (clinical details are given). 19 members of the kindred were examined; no evidence of thalassaemia was found, and none of the data were inconsistent with allelism between E and S (or A), though final proof was lacking. *Alan B. Raper*

NA-NAKORN, S. & MINNICH, Virginia. **Studies on Hemoglobin E. III. Homozygous Hemoglobin E and Variants of Thalassaemia and Hemoglobin E. A Family Study.** *Blood*. 1957, June, v. 12, No. 6, 529-38, 3 figs. [11 refs.]

Thalassaemia-haemoglobin-E disease is a doubly heterozygous state for the genes responsible for haemoglobins A and E, and for thalassaemia. However, though the gene for haemoglobin A is present and can be transmitted to the patient's offspring, the formation of haemoglobin A is suppressed in the phenotype, with the result that only haemoglobin E (and F) is found in the blood. It would therefore be difficult to distinguish a person of the genotype AE plus thalassaemia with the haemoglobin phenotype E plus F from one with thalassaemia-haemoglobin-E disease who was homozygous for haemoglobin E; the phenotype would also be E plus F.

This paper concerns itself with the possible differentiation between thalassaemia-homozygous-haemoglobin-E disease and thalassaemia-heterozygous-haemoglobin-E disease. A family is described in which the father was either of the genotype AE plus thalassaemia, or EE plus thalassaemia, and where the mother was homozygous for haemoglobin E. There were 8 children, and it could be expected that the two conditions might occur among them. Numerous other relatives were also examined. Unfortunately it was found impossible to differentiate between the two states from the genetic, clinical and haematological data available.

H. Lehmann

AKSOY, M., LEHMANN, H. & LIE-INJO LUAN ENG. **The Recognition of Haemoglobins A₂ and E.** [Correspondence.] *Lancet*. 1957, Apr. 13, 792-3, 1 fig.

Sickle-cell haemoglobin (haemoglobin S) and haemoglobin D, and haemoglobins E and A₂, form pairs of haemoglobins with identical electrophoretic properties. Differentiation between haemoglobins S and D is possible not only on the basis of solubility but also because haemoglobin D does not cause sickling. Distinction between the other pair of haemoglobins is, however, more difficult. Haemoglobin A₂ is found in small amounts in normal people and in larger amounts in thalassaemia. It is normally differentiated from haemoglobin A by open boundary and zone electrophoresis but an indication of its presence may be found by paper

electrophoresis—especially when thick paper is used and large amounts of haemoglobin are applied at the starting point. Staining with a protein stain may also make small amounts of haemoglobin A₂ more readily demonstrable.

Although A₂ has the same electrophoretic mobility as haemoglobin E, a guide to the differentiation between the two in haemoglobin AE heterozygotes or patients with thalassaemia who have both haemoglobins A₁ and A₂ present is that in a heterozygote for haemoglobins A and E the proportion of haemoglobin E present is seldom less than 20%, whereas the proportion of haemoglobin A₂ present in thalassaemia is seldom more than 15%. This difference helps in avoiding serious errors in carrying out mass surveys.

Taking this point into account the authors have reviewed their material gathered in surveys for haemoglobin E and find it unnecessary to alter their former estimates of its prevalence.

A. W. Woodruff

AGER, J. A. M. & LEHMANN, H. **Haemoglobin L: a New Haemoglobin found in a Punjabi Hindu.** *Brit. Med. J.* 1957, July 20, 142-3, 1 fig. [10 refs.]

The haemoglobin of an East Indian male, who was haematologically normal, was found to separate into 2 fractions at pH 8.6—normal haemoglobin, and 28% of a component that took up a position between control samples of haemoglobins S and G on zone electrophoresis on paper and on starch gels. There was no separation at pH 6.5. It was concluded that the solubility of the sample was normal [details are given]. The same haemoglobin constitution was found in the subject's mother, but not in his father, brother, and sister, who were normal.

The separate identity of this variant having been established, it is to be named haemoglobin L.

Alan B. Raper

VENOMS AND ANTIVENENES

SCHENONE, H., NIEDMANN, G., BAHAMONDE, L. & BONNEFOY, J. Algunas alteraciones cardiovasculares observadas en el latroductismo. [**Cardiovascular Manifestations in Latroductism**] *Bol. Chileno de Parasit.* 1957, Apr.—June, v. 12, No. 2, 29-30, 2 figs. [10 refs.]

The English summary appended to the paper is as follows:—

“Cardiovascular manifestations were studied in six male patients bitten by the spider *Latrodectus mactans*. Precordial pains, anxiety and hypertension were observed in almost all our patients. Transitory electrocardiographical changes were found in five of them. These changes corresponded to alterations of the S-T segment and T wave.”

HICKS, A. **Coral Ulcer.** *East African Med. J.* 1957, Apr., v. 34, No. 4, 121-31, 7 figs.

The author, in Nairobi, has been impressed by the numbers of returning holiday-makers from the East African coast who require treatment for intractable ulcers on the feet and legs resulting from contact with living coral. Within 24 hours of such contact a painful sloughing ulcer may develop, which discharges thin, greyish pus and is often accompanied by cellulitis, lymphangitis and inflammation of the regional glands. A little later constitutional symptoms develop, which are often severe; these comprise malaise, headache and low pyrexia. *Staphylococcus albus* may be grown from the lesion, but this is certainly not the primary aetiological agent. Systemic treatment by antibiotics is ineffective, and the local application of penicillin and sulphathiazole powder does not improve healing and is unwise in view of the risks of sensitization. The ulcer usually responds slowly to rest, elevation, saline compresses, kaolin poultice, magnesium sulphate paste or strapping with Elastoplast: the last usually proves the simplest and most effective treatment. One month's immobilization is often required, and complete healing may take a further 4 weeks.

There can be little doubt that a histiotoxic agent derived from living coral is the primary aetiological agent, and thus constitutes a recreational hazard to goggle and aqualung divers. [It has long been known to pearl divers in the Persian Gulf.]

The stony corals, or Madreporaria, are an order of the class Actinozoa of the phylum Coelenterata, which also includes the sea anenomes and jelly-fish whose stinging potentialities are notorious. The Madreporaria are confined to warm seas whose temperature does not fall below 68°F. (20°C.), and are therefore found in a zone extending to 30° on either side of the Equator. They grow from the high water mark to a depth of some 20 fathoms.

The stinging capsule or nematocyst is a highly specialized cell embedded in profusion in the ectoderm of the tentacles. It comprises a venom-containing sac into which is invaginated a hair-like, hollow lance; this is forcibly evaginated in response to a tactile stimulus applied to a short projecting trigger. The lance is too fragile always to penetrate the intact human skin, but is able to inject its toxin wherever the protecting epidermis has been lost by abrasion. The composition of the coral toxin is not known, but it is thought to contain a vesicating, cantharidine-like substance.

[This most fascinating and well-illustrated paper will amply repay those who study it in the original.]

J. H. Walters

TOXOPLASMOSIS

CHERNIN, E. & WELLER, T. H. **Further Observations on the Growth of *Toxoplasma gondii* in Roller Tube Cultures of Mouse and Primate Tissues.** *J. Parasitology*. 1957, Feb., v. 43, No. 1, 33-9, 3 figs.

The RH strain of *Toxoplasma gondii* was studied in 23 successive passages in mouse embryo cultures and the KM strain in 13. The infectivity of the organism to mice remained unchanged after this prolonged cultivation. On inoculation there is a lag period of usually 3 days; from the 3rd to 6th days a moderate number of toxoplasms occur, often in sheet-like plaques, and cause much cellular destruction; from the 7th to 10th days the numbers decline; and after 10 weeks no *Toxoplasma* or cells remain. Replacement of nutrient medium prolongs the multiplication period.

The course of intracellular development was followed by removing material after different hours: after 6 hours the infection rate was low and half the cells contained single parasites, the other half up to 10; 24-hour preparations showed numerous parasites usually in multiples of 2. Fibroblast and epithelial-like cells were invaded in mouse embryo cultures, squamous epithelial cells in human foreskin cultures; other human cells, and testicular cells of monkeys (which showed beautiful rosettes), were also susceptible. Apart from a vacuole around the parasites, little or no cellular change was detected prior to dissolution. Culture fluid was not toxic to growth.

P. C. C. Garnham

FULTON, J. D. & SPOONER, D. F. **Preliminary Observations on the Metabolism of *Toxoplasma gondii*.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1957, Mar., v. 51, No. 2, 123-4.

The metabolism of *Toxoplasma gondii* in the free state was studied from suspensions obtained from the peritoneal exudate of various animals 3 days after infection. Rabbits and rats were found to be useless as a source of parasites, cotton rats were best, while merions, guineapigs, hamsters, white mice and multimammate rats were inferior. The peritoneal fluid was mixed with citrate saline, centrifuged, and the deposit suspended in a medium containing 0.2% glucose in 1 part horse serum and 9 parts phosphate saline at a pH of 7.4. Intracellular parasites were freed by shaking with glass beads. The suspension was standardized by the fowl red blood cell technique. Any white cells were removed by filtration through a sintered glass filter and red cells after agglutination by the appropriate antiserum. 15 cotton rats yielded about 5×10^9 organisms.

Toxoplasma gondii was found to consume oxygen for at least 2 hours, when suspended in the above medium, at a rate of 12 microlitres/10⁸ parasites per hour. Carbon dioxide was produced and the respiratory

quotient in two experiments was 1.14 and 1.03. Glucose, which is the major substrate for respiration, was utilized at the rate of 0.3 micro-moles/ 10^8 parasites per hour. Respiration was inhibited by cyanide.

P. C. C. Garnham

GOLDMAN, M. **Staining *Toxoplasma gondii* with Fluorescein-Labelled Antibody. I. The Reaction in Smears of Peritoneal Exudate.** *J. Exper. Med.* 1957, June 1, v. 105, No. 6, 549-56, 2 figs. **II. A New Serologic Test for Antibodies to *Toxoplasma* based upon Inhibition of Specific Staining.** *Ibid.*, 557-73. [12 refs.]

I. The author has devised a new technique which confirms the specificity of the methylene blue dye test for infections with *Toxoplasma gondii*. A human serum with a titre of 1 in 4,000 in the dye test was treated with ammonium sulphate to obtain the globulin fraction which was then "labelled" with fluorescein. Control sera with a negative dye test were treated in the same way. Films of the organism were then prepared by exposing 0.5 to 1 cc. of infected peritoneal exudate to 10 cc. of 1% formol saline for half an hour; centrifuging the suspension at 500 r.p.m. for 5 minutes to throw down the heavier particles and at 1,500 r.p.m. to throw down the organisms; suspending the sediment in 3 cc. saline and making smears on slides over an area of about 4-5 mm. in diameter. The smears were stored at -20°C . The antibody antigen reaction was obtained by pouring 0.04 cc. of the labelled antibody on to the slide, keeping for 1 hour in a wet chamber at 37°C . and washing in saline for 10 minutes and in water for 5 minutes. After drying, the film was mounted in a drop of buffered glycerine (pH 8.0) and was examined under the fluorescent microscope.

Bright fluorescence, particularly of the periphery, was produced in the *Toxoplasma* exposed to labelled immune sera, but not in the negative controls. Staining was inhibited if the films were treated first with non-labelled immune serum, but was not inhibited with non-labelled normal serum. Cultures of *Trypanosoma cruzi* were substituted for *Toxoplasma gondii* and gave a low level fluorescence. [It would have been interesting to have treated *Sarcocystis* spores in the same way, because this protozoon is possibly more closely related to *Toxoplasma* than *T. cruzi*.]

Toxoplasma gondii washed in formalin (0.1%) remained viable for 20 minutes, but 1% formalin killed nearly all the organisms in 30 minutes.

II. The above paper demonstrated that the fluorescein antibody antigen reaction is inhibited if the antigen is first exposed to immune serum. The author uses this phenomenon to detect the presence of immune bodies in unknown sera. He first showed that the simultaneous application of labelled and unlabelled antisera gave more consistent results than their application in sequence; next he found that it was better to dilute the labelled antiserum, usually 1 in 2. The reaction was then tested in

150 sera and the results were compared with the dye test. Provided that the smears were properly dried after removal from the freezing chamber and that they were exposed to the sera for one hour, a good degree of correlation with the dye test was obtained at titres above 1 in 256. The reaction was then tested in 50 sera from patients with congenital toxoplasmosis and agreement here was much closer: 27 were positive in the dye test and 30 were positive in the inhibition test. 100 sera were tested by the complement-fixation reactions, and these showed 24 times fewer positives than the inhibition test.

The inhibition test was employed on sera from 111 animals infected with a variety of organisms, including bacteria, helminths, viruses and *Trypanosoma gambiense* and *Entamoeba histolytica* [but unfortunately not *Sarcocystis* or *Trichomonas*] and none showed a positive result.

The inhibition test is better than the dye test because (1) it uses a killed standardized antigen, (2) it does not require accessory factor, and (3) its results are less variable. P. C. C. Garnham

CATHIE, I. A. B. & CECIL, G. W. **Sarcosporos and Toxoplasma Serology. An Investigation of their Alleged Cross-Reaction.** *Lancet.* 1957, Apr. 20, 816-18.

In this work the authors attempted—unsuccessfully—to repeat the work of AWAD [this *Bulletin*, 1955, v. 52, 294] on the use of “sarcosporos” in the Sabin-Feldman dye test for toxoplasmosis. 23 human sera of known toxoplasma-antibody content were set up with sarcosporos and all gave a positive reaction, but only one-third to “toxoplasms”; 93 other human sera gave a similar result. If the sera were inactivated at 56°C. for 30 minutes all the tests became negative if fresh sarcosporos were used, but remained positive if sarcosporos a month old were used. Inactivation had no effect on the classical dye test (with toxoplasms).

A guineapig immunized with *Sarcocystis* antigen gave a positive complement-fixation reaction and a false positive dye test. Of 10 sheep sera, 6 gave a positive complement-fixation test and all a false positive dye test (before inactivation).

The authors are thus unable to confirm Awad's findings in regard to the substitution of sarcosporos in the dye test, but they point out the perplexing nature of the reaction which old sarcosporos give in this test, and which yet remains to be explained. P. C. C. Garnham

SIMITCH, T., PETROVITCH, Z., BORDJOCHKI, A. & POP-CENITCH, S. Contribution à la connaissance de la biologie de *Toxoplasma gondii* chez le chien (Note préliminaire). [Contribution to the Knowledge of the Biology of *Toxoplasma gondii* in the Dog. Preliminary note] *Arch. Inst. Pasteur d'Algérie.* 1957, Mar., v. 35, No. 1, 24-30.

30 dogs of different ages were inoculated by various routes with a strain of *Toxoplasma gondii* originally isolated from an Algerian dog. Evidence

of infection was found either by direct examination of the animal or by subinoculation of suspensions of organs into *Citellus citellus* (which the authors had previously shown to be highly susceptible to the organism—this *Bulletin*, 1957, v. 54, 876). 2 of 6 puppies (8–10 days old) showed a latent infection after oral infection. 4 of 6 puppies (8–20 days old) showed a latent infection after subcutaneous inoculation. 2 of 5 puppies (14–24 days old) died of acute toxoplasmosis and 1 of the remainder developed a latent infection after intraperitoneal inoculation. 7 of 10 young dogs died after suboccipital inoculation but in only 2 of them was the organism directly found (in the brain); in the others it was demonstrated by subinoculation into ground squirrels; all 3 remaining dogs had a latent infection. 3 older dogs (2 years) were inoculated intravenously—one exhibited *Toxoplasma* in the blood 2 days later, but the infection failed to become established.

P. C. C. Garnham

BEVERLEY, J. K. A. & FRY, B. A. **The Treatment of Experimental Toxoplasmosis in Rabbits.** *Brit. J. Pharmacol. & Chemotherapy*. 1957, June, v. 12, No. 2, 185–8, 2 figs. [13 refs.]

The authors have compared the efficacy of sulphadimidine, pyrimethamine and dapsone (diaminodiphenylsulphone) in the treatment of rabbits infected with *Toxoplasma*. In all, 27 rabbits of weight 2.0 to 3.0 kgm. were used and arranged in groups of 3 before infection intradermally with about 80,000 parasites of the RH strain of *T. gondii*. Treatment was begun 2 hours later and continued thrice daily for 9 days, with gelatin capsules and suspensions of drug in water as well as intravenous doses of the soluble salt. The method used for drug estimation was that described in this *Bulletin*, 1951, v. 48, 268.

Because of the fact that some rabbits acetylate certain sulphonamides more quickly than others the results obtained with this group of substances were not consistent. The successful treatment of toxoplasmosis in rabbits by SABIN and WARREN [*ibid.*, 1943, v. 40, 638] with sulphathiazole led the present authors to compare the levels reached in the blood with those after administration of sulphadimidine. With the former higher levels were reached. Because of the variations in levels of free sulphadimidine in the blood of rabbits after treatment, its value in treatment of these animals is doubtful, although satisfactory results are obtained in mice. Pyrimethamine in high doses was not effective in treatment of rabbits whereas dapsone was.

J. D. Fulton

BEVERLEY, J. K. A. & FRY, B. A. **Sulphadimidine, Pyrimethamine and Dapsone in the Treatment of Toxoplasmosis in Mice.** *Brit. J. Pharmacol. & Chemotherapy*. 1957, June, v. 12, No. 2, 189–93, 2 figs. [13 refs.]

It has been shown by other workers [this *Bulletin*, 1953, v. 50, 980; 1956, v. 53, 655] that sulphonamides are effective in treatment of

toxoplasmosis in mice and that there is a synergism between these substances and pyrimethamine. Using infected mice the authors have attempted to assess the relative value of sulphadimidine, dapsone (diaminodiphenylsulphone) and pyrimethamine in short term experiments, and to find whether synergy exists among them. Their therapeutic indices were also determined. Very large numbers of mice, up to 300 in a single experiment, were used and infected by allowing droplets containing about 20,000 toxoplasms to fall on the nasal mucous membrane. The drugs used were incorporated in diet, and treatment, begun immediately after inoculation, was continued for 1 to 4 weeks. Toxicity had been determined previously by noting the amount of any drug which prevented gain in weight. The relapse time, survival time and state of infection were determined after each drug regimen. The period of observation lasted 4 weeks after cessation of treatment. Brain, spleen and liver suspensions from mice at autopsy, to which penicillin and streptomycin had been added, were inoculated into fresh mice to find if infection persisted.

The results indicated that sulphadimidine was more active than pyrimethamine or dapsone alone in the acute stages of the disease, but relapses occurred. At toxic levels pyrimethamine produced cures. Dapsone was less effective. Sulphadimidine and pyrimethamine acted synergically and effected cures. Dapsone and pyrimethamine also acted synergically but were less effective than the first pair. The mode of action of these drugs is discussed.

J. D. Fulton

DERMATOLOGY AND FUNGUS DISEASES

See also p. 1244, DOBSON & LOBITZ, **Some Histochemical Observations on the Human Eccrine Sweat Glands. II. The Pathogenesis of Miliaria.**

ANDLEIGH, H. S. **Etiology of Maduromycosis in India.** *Mycopathologia*. The Hague. 1957, June 25, v. 8, No. 2, 138-53, 7 figs. [12 refs.]

ANDLEIGH, H. S. **In vitro Study of Antifungal Activity of Pentamidine and Stilbamidine.** *Mycopathologia*. The Hague. 1957, June 25, v. 8, No. 2, 135-7.

The author, in India, tested 5 cultures of *Madurella mycetomi* isolated from cases of "black granule" maduromycosis, for sensitivity to pentamidine and stilbamidine. The liquid medium employed was brain heart infusion with added penicillin (20 units/ml.) and streptomycin (50 units/

ml.). To this the 2 drugs were added directly in serial concentrations of 0.01 mgm./ml. to 0.3 mgm./ml. of medium. Pentamidine inhibited growth of *M. mycetomi* in a concentration of 0.1 mgm./ml., but stilbamidine inhibited only 3 of the 5 cultures at 0.2 mgm./ml. *In vivo* trials are planned and a further report promised.

H. J. O'D. Burke-Gaffney

ZIPRKOWSKI, L., ALTMANN, G., DALITH, F. & SPITZ, U. *Mycetoma pedis*.

Four Cases treated with Streptomycin. *Arch. Dermat.* 1957, June, v. 75, No. 6, 855-63, 10 figs.

The authors describe 4 cases of mycetoma of the foot in Israel, affecting 3 men aged respectively 35, 36 and 45 years and a woman aged 44, all natives of the Yemen. In 3 of the patients the disease was caused by *Nocardia madurae* and in the other one by *Nocardia somaliensis*. The bacteriological diagnosis was confirmed by culture in all cases except 1 in the *N. madurae* group.

The strains of *N. madurae* were found to be sensitive *in vitro* to streptomycin and tetracycline, but the *N. somaliensis* strain only to tetracycline.

One patient in the *N. madurae* group, whose disease was of 10 years' duration with involvement of the tarsus and metatarsus, was treated unsuccessfully with trisulphapyrimidines (Trisulpha) to a total of 47 gm. in 10 days. The treatment was then changed to streptomycin, 3 gm. daily, and after administration of 60 gm. there was definite clinical improvement. The dosage was then reduced to 2 gm. and later to 1 gm. daily. At the end of 6 months, when 165 gm. of streptomycin had been given, clinical cure was complete and the use of the affected limb restored, but X-ray examination showed no early improvement in the bone lesions. The only "side effect" from the treatment was a vestibular disturbance which developed after 80 gm. had been given. No relapse occurred during follow-up observations over a period of 6 years.

In the second *N. madurae* case the bones were not involved. Much of the infected soft tissues was removed by surgical excision, and streptomycin was given at a dosage of 1 gm. daily to a total of 54 gm. This caused complete cure, confirmed by a 2½-year follow-up.

The third patient in the *N. madurae* group was treated with streptomycin, 1 gm. daily, but treatment was abandoned because of a severe psychosis, attributable to the treatment, which appeared after 40 gm. had been administered.

In the fourth patient the disease, of a severe type with involvement of the tarsus and metatarsus, was caused by *N. somaliensis* and was of 7 or 8 years' duration. Streptomycin, 1 gm. daily, was given to a total of 134 gm. This caused apparent clinical cure but relapse occurred 5 months after discharge from hospital. A further course of streptomycin, 22 gm., supplemented by chlortetracycline, 12 gm., in 22 days completed

the clinical cure and an X-ray examination made a year later showed regression of the osseous lesions.

Descriptions of the 2 micro-organisms in culture are given.

J. T. Duncan

HÜGENHOLTZ, P. G. Coccidioidomycosis. Enkele opmerkingen naar aanleiding van 37 geobserveerde gevallen. [**Observations on 37 Cases of Coccidioidomycosis**] *Nederl. Tijdschr. v. Geneesk.* 1957, June 29, v. 101, No. 26, 1204-12, 6 figs. [33 refs.]

The English summary appended to the paper is as follows:—

“A survey of the present day knowledge of coccidioidomycosis is given. It is increasingly important—even in non-endemic parts of the world—to consider this disease in the differential diagnosis of isolated pulmonary residuals. Intracutaneous coccidioidin, serology, sputum culture and microscopical analysis of the resected lesion are the available diagnostic aids. A series of 37 primary cases observed in Arizona is described.”

HEAT STROKE AND ALLIED CONDITIONS

LADELL, W. S. S. **Disorders due to Heat.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1957, May, v. 51, No. 3, 189-207, 4 figs. [54 refs.] Discussion 207-16 [WALTERS, J. H.; STAMM, W. P.; LEITHEAD, C. S.; GOOD, M. G.; CROWDEN, G. P.; THOMSON, M. L.; WEINER, J. S.; LADELL, W. S. S. (in reply)].

The minor heat disorders are given as sunburn, prickly heat and heat syncope; the major, as heat exhaustion, heat cramps (both disorders of electrolyte and water metabolism), tropical anhidrotic asthenia and hyperpyrexia (both failures of heat regulation).

Sunburn. Exposure to ultra-violet light results in erythema, pain and, later, increased pigmentation and defective sweating.

Prickly heat. Dr. Ladell's account agrees closely with that of SARGENT and SLUTSKY [this *Bulletin*, 1957, v. 54, 1125].

Heat Syncope. The extra demand for skin blood flow required for heat loss contributes to the more ready occurrence of syncope. Resistance to this kind of collapse is increased after acclimatization to heat.

Heat exhaustion. Exhaustion is accompanied by pale, sweating skin, slightly raised body temperature and high pulse rate. The patient is dehydrated, the urine is scanty, deeply pigmented and free from chloride. There is haemo-concentration, fall in blood electrolytes and, in most cases, muscle cramps.

Heat cramps. These are the consequence of a low concentration of sodium in the extracellular fluid (ECF) and have always been associated with hard work in the heat. They are promptly relieved by intravenous saline.

The aetiology of heat exhaustion and heat cramps is now discussed at length. The author considers the chronic loss of weight, found so universally in the heat, to be due to failure to drink enough to replace losses from sweating. The body water may be reduced by about 2 litres at the expense of digestive juices before intracellular fluid (ICF) is affected. It is the loss of this "hump" which renders man susceptible to heat exhaustion.

Both intra- and extra-cellular fluid volume (ICFV and ECFV) must be maintained for health. During acute exposure to heat, when water but no salt is taken, the ICFV is maintained and any deficit falls on the ECFV, leading to the usual signs of salt deficiency; when salt but little water is taken the ICFV falls and collapse ensues. Thus the correct treatment is plenty of water but a controlled supply of NaCl.

The sodium-conserving action of adrenal cortical extracts (notably aldosterone) on the renal tubules is paralleled by an electrolyte-saving effect on the sweat gland. The reduction in sweat electrolyte during acclimatization to heat is apparently dependent on normal adrenal gland function. When dietary sodium is restricted or when the ECFV falls aldosterone secretion is stimulated and *vice versa*. Retention of sodium brings about retention of water and *vice versa* so that osmotic pressure and fluid volume are normally well controlled. However, where one of these has to be sacrificed, osmotic pressure is allowed to rise, leading to the abnormal fluid-salt balance found in heat exhaustion.

The author considers salt to be a luxury indulged in first by prehistoric man who rapidly became addicted to it, thereby losing the efficiency of his aldosterone mechanism.

Tropical anhidrotic asthenia. The account here resembles that of Sargent and Slutsky [*loc. cit.*].

Hyperpyrexia. The outstanding feature is a burning dry skin. Unconsciousness supervenes when body temperature reaches 105–107°F. Death occurs unless there is active treatment; at autopsy only cerebral oedema and petechial haemorrhages in the hypothalamus are consistently found.

Treatment is by cooling the patient to 101°F. by wrapping in a wet sheet and fanning briskly.

The author believes that the cause of failure of sweating is sweat-gland fatigue: as rectal temperature increases sweating falls off exponentially. He shows by extrapolating his data that at 110°F. body temperature the sweat rate would lie between 0.9 and 0.35 ml./min., *i.e.*, 0 for all practical purposes. If the environment is sufficiently hot this vicious, albeit physiological, circle may be initiated by heavy physical effort, poor air movement, too much clothing, prickly heat or sunburn.

In discussion, Dr. J. H. WALTERS described 36 cases of hyperpyrexia seen in Kuwait in the hot summer of 1953. Many were obese immigrants who had had salt-deficiency dehydration with anorexia, headache, lassitude and muscular cramps. Some were pilgrims, healthy on arrival, who had been confined in intolerably hot custom sheds. There were 16 deaths; 3 survivors showed cerebellar damage.

Patients with arsenical exfoliative dermatitis and with prickly heat were in great danger because of the inhibition of sweating.

Group Captain W. P. STAMM reported on the recommendations on nomenclature of the heat disorders made by a committee appointed by the Council of the Royal Society of Tropical Medicine and Hygiene.

Dr. C. S. LEITHEAD described 62 cases of heat illness occurring among 62,500 sailors at Mina, Kuwait, from May to September 1956. 21 of these had heat syncope; 30 had salt- and water-deficiency heat exhaustion; 5 had hyperpyrexia; 1 patient had anhidrotic heat exhaustion. The high proportion of heat exhaustion was attributed to lack of acclimatization and to severe heat stress in engine room and galley. However, in 80% of all heat casualties examined the intake of NaCl was judged to be inadequate.

Dr. M. G. GOOD drew attention to the role of potassium, which, in excess, caused increased irritability of muscle and general cramps. Hypopotassaemia resembled the clinical picture of tropical anhidrotic asthenia.

Professor G. P. CROWDEN raised the point that in view of air conditioning in modern aircraft and rapidity of travel, some degree of artificial acclimatization to heat may be desirable before flying. What thermal conditions and exercise would be suitable for this purpose in young men?

Dr. M. L. THOMSON suggested that the pathological process was identical in heat cramp and salt-deficiency heat exhaustion: if the salt-deficient person worked he got cramps and then would be diagnosed "heat cramps". The term "heat cramps" might be dropped and "extracellular" and "intracellular dehydration" used where salt and water deficiency respectively predominate.

He felt it would be dangerous to alter the present policy of advocating increased salt intake in the heat.

Dr. J. S. WEINER stressed that heat syncope was of vasovagal type with bradycardia and sudden increase in forearm blood flow. It was common among Bantu and resulted in their rejection during heat selection tests.

A moderate salt supplement should be given when there is a sudden change in work conditions causing profuse sweating. *M. L. Thomson*

DOBSON, R. L. & LOBITZ, W. C., Jr. **Some Histochemical Observations on the Human Eccrine Sweat Glands. II. The Pathogenesis of Miliaria.** *Arch. Dermat.* 1957, May, v. 75, No. 5, 653-66, 10 figs. [14 refs.]

This important study of experimentally produced miliaria was made in order to clear up certain discrepancies between the natural and artificial lesion.

Ethyl chloride and phenol were found to damage the human epidermis in such a way that, when sweating was provoked one week later, thick-walled irregular bullae appeared on the injured area. In the epidermal roof of these bullae were degenerated eccrine sweat-gland ducts; in the floor were newly regenerated sweat-ducts. This type of lesion, produced by strong chemicals, heat or cold, is not a true miliaria crystallina.

One week after iontophoresis with distilled water at the anode, sweating produced vesicles in which the terminal sweat-duct in the roof (in this case consisting of stratum corneum only) was dilated and filled with Schiff-positive, diastase-resistant material. This vesicle was indistinguishable from clinical miliaria crystallina. There was no keratin plug.

Further serial biopsies were carried out at 1, 3, 5 and 7 days after a heavy bout of sweating produced 1 week after injury by iontophoresis. As a result of this study the following theory is advanced to account for the genesis of natural miliaria.

A hyperkeratotic or parakeratotic plug undoubtedly causes the poral occlusion in miliaria rubra. This, however, is a secondary effect of injury occurring at least 3 days previously and associated with the first plugging of the duct (or first attack of miliaria) by Schiff-positive, diastase-resistant material. About 1 week after injury the degenerated terminal sweat-duct, seen as a parakeratotic mass, blocks the newly regenerated sweat-duct unit, setting the stage for the next episode of miliaria. The sequence may continue indefinitely if sweating is induced at weekly intervals. The obstruction tends to become deeper, which accounts for the eventual production of miliaria profunda. M. L. Thomson

MISCELLANEOUS DISEASES

FAIN, A. & FALAISE, A. A propos du rhinosclérome au Ruanda-Urundi. [**Rhinoscleroma in Ruanda-Urundi**] *Ann. Soc. Belge de Méd. Trop.* 1957, Feb. 28, v. 37, No. 1, 67-9, 2 figs. on 2 pls.

The English summary appended to the paper is as follows:—

“Within a period of four months, four cases of rhinoscleroma have been diagnosed in Ruanda-Urundi, where the affection appears to be far from rare, but is probably mistaken for yaws; the diagnosis has been established by histological examination, which shows a characteristic aspect. This work is illustrated by a photograph.”

STEIN, H. **Veno-Occlusive Disease of Liver in African Children.** *Brit. Med. J.* 1957, June 29, 1496-9, 2 figs. [10 refs.]

The clinical records are given of 3 African children aged 5, 12 and 14 months who were admitted to hospital acutely ill with ascites, enlarged livers, but no jaundice. All 3 died and at each necropsy the centrilobular veins of the liver showed acute oedematous internal thickening with almost complete occlusion of the lumen. A pathological diagnosis of veno-occlusive disease of the liver was made.

None of the children were strikingly undernourished. There was no history to suggest that any herbs or plants [such as *senecio*] had been taken. However, these are frequently given by witch-doctors and the fact is concealed when the child is brought to hospital. [See also this *Bulletin*, 1956, v. 53, 1054.] *R. Passmore*

BRAS, G., BERRY, D. M. & GYÖRGY, P. **Plants as Aetiological Factor in Veno-Occlusive Disease of the Liver.** *Lancet.* 1957, May 11, 960-62, 6 figs. [30 refs.]

This paper contains 6 excellent photomicrographs of occlusive lesions in branches of hepatic veins; the livers were taken from horses, cows and a calf poisoned with one or other of the herbs *Crotalaria* (rattle-box) or *Senecio* (ragwort). The histological picture appears very similar to that previously described in the human liver and known as veno-occlusive disease in man. It is postulated that herbal infusions of *Crotalaria*, which are taken by the Jamaican population for medicinal and other purposes, may be one of the aetiological factors responsible for veno-occlusive disease of the liver. [See also this *Bulletin*, 1957, v. 54, 77.]

R. Passmore

SACHDEV, S., SACHDEV, J. C. & SINGH, R. C. **Serum Amylase Values in Liver Dysfunction.** *J. Indian Med. Ass.* 1957, Apr. 1, v. 28, No. 7, 304-6, 2 figs.

The serum amylase values were found to be low in a group of 76 patients of all ages suffering from liver diseases. The levels of serum amylase were not related to the degree of liver enlargement, but low levels of plasma protein were associated with low levels of amylase.

R. Passmore

SINGH, A., PRAKASH, C. & BALASUBRAHMANYAN, M. **Endomyocardial Fibroelastosis. Case Report with Review of the Literature.** *Indian J. Med. Sci.* 1957, May, v. 11, No. 5, 332-6, 5 figs. on pl. [22 refs.]

ENTOMOLOGY AND INSECTICIDES: GENERAL ZOOLOGY

[Papers on the toxic effects of insecticides in man are abstracted in the *Bulletin of Hygiene* under the general heading of Occupational Hygiene and Toxicology.]

GRJEBINE, A. Données récentes sur les Culicidés d'Afrique Equatoriale Française. 1. Culicines. [**Recent Data on Mosquitoes of French Equatorial Africa. I. Culicines**] *Ann. Parasit. Humaine et Comparée*. 1957, Apr.-June, v. 32, No. 3, 331-41. [16 refs.]

RAMACHANDRA RAO, T. & RAJAGOPALAN, P. K. **Observations on Mosquitoes of Poona District, India, with special reference to their Distribution, Seasonal Prevalence and the Biology of Adults.** *Indian J. Malariology*. 1957, Mar., v. 11, No. 1, 1-54, 1 map & 8 charts. [13 refs.]

It is important that large numbers of mosquitoes should be collected and studied to determine their role as the vectors of viruses in nature. The present studies deal exclusively with adult mosquitoes of the Poona District of India. First the topography, climate and hydrological features of the District are described and a map shows the areas studied. Then the observations are discussed under 5 headings: genera and species, seasonal prevalence, attraction to man, attraction to baits other than man, and detailed notes on species.

Nearly 50,000 mosquitoes were recorded in 89 species (including 11 undetermined) belonging to 11 genera; 24 species were recorded for the first time and 38 other species though not collected may be expected to occur in the district. 5,355 mosquitoes of 39 species were caught alighting on man of which 36 species took blood meals; of these, 3 species of *Aedes* (*Stegomyia*) accounted for 4,693; they were *Aedes* (*S.*) *albopictus*, *A.* (*S.*) *vittatus* and *A.* (*S.*) *w-albus*.

In portable traps with birds and small mammals as bait a total of 769 mosquitoes were taken on 59 occasions. *Culex fatigans* was most frequently taken on all baits. The others were *C. bitaeniorhynchus*, *Mansonia crassipes*, *C. vishnui*, *C. mimulus* and *Aedes vittatus*.

Aedes (*S.*) *aegypti* was taken only once and that a male; no females and no larvae were found. The only mosquito found in houses in Poona City was *Culex fatigans*. Both *Mansonia* (*Mansonioides*) *annulifera* and *M.* (*M.*) *uniformis* occur in Poona District but are rare.

20 species of *Anopheles* were taken; 3 of them, *A. aitkeni*, *A. culiciformis* and *A. karwari* were not reported by VISWANATHAN in 1950 and 1 species, *A. varuna*, was not collected this time. 13 species were found biting man: *A. barbirostris*, *A. culicifacies*, *A. culiciformis*, *A. fluviatilis*, *A. hyrcanus*, *A. jamesi*, *A. karwari*, *A. maculatus*, *A. moghulensis*, *A. subpictus*, *A. tessellatus*, *A. theobaldi* and *A. vagus*.

Besides species which have been recorded as responsible for the

transmission of viruses in other parts of the world, recent work in Poona has led to the isolation of a virus of the West Nile-Japanese B complex in Southern India from *C. vishnui* and an unidentified virus from *C. bitaeniorhynchus*. *C. vishnui* especially may have an important role in the transmission of neurotropic viruses in India. H. S. Leeson

CHEN, H. H. **Keys to the 19 Species of Mosquitoes common in Taiwan (Formosa), China.** *J. Formosan Med. Ass.* 1956, Oct., v. 55, No. 10, 487-93, 2 folding diagrams.

DASGUPTA, B. & RAY, H. N. **The Intranuclear Inclusions in the Mid-Gut of the Larva of *Anopheles subpictus*.** *Parasitology.* 1957, June, v. 47, Nos. 1/2, 194-5.

MOUCHET, J., GARIOU, J. & RIVOLA, E. Observations sur la biologie d'*Anopheles smithi* var. *rageai* Mattingly et Adam 1954, vecteur d'un *Plasmodium* de mammifère aux environs de Yaoundé (Sud-Cameroun). [**The Biology of *A. smithi* var. *rageai*, a Vector of a Mammalian *Plasmodium* around Yaoundé**] *Bull. Soc. Path. Exot.* 1957, Jan.-Feb., v. 50, No. 1, 157-64, 2 figs. on 2 pls. & 1 map.

The authors studied the biology of *Anopheles smithi* var. *rageai* around Yaoundé, Cameroon. Localities are shown on a map and the larval and adult habitats are shown in photographs.

Larvae are most abundant in rock- and tree-shaded patches of clear, spring-like water in ravines. Adults are found among the trees and bushes, below the cliffs, in cracks in rocks, between fallen rocks and among rock rubbish and below overhanging rocks.

Dissections of 343 female mosquitoes from different places showed varying rates of infection (0-50%) with a mammalian *Plasmodium*. Precipitin tests on 67 stomach contents revealed that porcupine blood was the chief diet. Several days after infected mosquito material had been injected into 2 clean porcupines parasites were seen in their blood. In 2 hut experiments the mosquito was not obtained in the huts by day or night and the observers were not bitten though the species was plentiful outside.

It is therefore concluded that at the places and times studied *Anopheles smithi* var. *rageai* is not anthropophilic and is not a vector of the malaria parasite of man. H. S. Leeson

SPIELMAN, A. **The Inheritance of Autogeny in the *Culex pipiens* Complex of Mosquitoes.** *Amer. J. Hyg.* 1957, May, v. 65, No. 3, 404-25, 9 figs. [Numerous refs.]

This is an account of a laboratory investigation into the subject given in the title. Interested readers should consult the original paper.

The following are some points extracted from the author's summary and conclusions. Anautogenous females of the *Culex pipiens* complex undergo an ovarian diapause which is characterized by the deposition of an insufficient quantity of yolk to pack the oöcyte. Autogenous development is not affected by mating but fewer eggs are developed by virgin females than by mated ones and fewer are formed into rafts. Chilling halts ovarian development but it is resumed when normal temperatures return. Pupal crowding inhibits autogeny.

The findings suggest that autogeny is probably inherited on 2 pairs of chromosomes (rather than on 3) and that crossover may occur between the sex and the autogeny-controlling factors. H. S. Leeson

TWOHY, D. W. & ROZEBOOM, L. E. **A Comparison of Food Reserves in Autogenous and Anautogenous *Culex pipiens* Populations.** *Amer. J. Hyg.* 1957, May, v. 65, No. 3, 316-24, 2 figs. [15 refs.]

"Under comparable conditions of environment and nutrition, molestus larvae required a slightly longer period to complete their development, and gave rise to larger adults than did pipiens.

"The molestus pupae and adult females contained larger amounts of lipids, glycogen and nitrogen than did pipiens. The larger molestus also contained a higher proportion of lipids and glycogen, but a lower proportion of nitrogen than did pipiens.

"The rates of utilization of these components was the same in the two forms.

"By the time that unfed molestus females deposit their autogenous eggs, pipiens females have used up all their lipid and glycogen reserves and the rate of loss of glycogen and lipids in pipiens may preclude their utilization in the formation of more than a small amount of yolk. The larger reserves in molestus supply an adequate amount of material for the developing ovaries, and permit survival of the females through the gestation period. However, it is evident that the greater reserves accumulated by molestus are not the result of environment, but that this is an inherent ability which may involve hormones or a specific food factor."

DOW, R. P., REEVES, W. C. & BELLAMY, R. E. **Field Tests of Avian Host Preference of *Culex tarsalis* Coq.** *Amer. J. Trop. Med. & Hyg.* 1957, Mar., v. 6, No. 2, 294-303, 2 figs.

"In comparative tests with baited traps slowly rotated about a common vertical axis, comparable numbers of *Culex tarsalis* were attracted to birds of the same size whether of the same or different species, while the number attracted to birds of different size was proportional to their size.

"*C. tarsalis* engorgement rates were independent of attraction rates and size of bird, but they varied for different bird species and for different individuals of the same species. Engorgement rates on individual birds were usually consistent, with only a few instances of night-to-night differences. A combination of the host's attractiveness and acceptability to *C. tarsalis* undoubtedly influences the biting attack rates on avian hosts.

"A depression of the engorgement of *C. tarsalis* on chickens was found to be correlated with increased numbers of mosquitoes.

"*C. tarsalis* is attracted to and feeds on a wide range of avian and mammalian species exposed in traps under field conditions."

GILBERT, I. H., GOUCK, H. K. & SMITH, C. N. **Diethyltoluamide: New Insect Repellent.** *Soap*. New York. 1957, May & June, v. 33, Nos. 5 & 6, 115-17, 129-33; 95-9, 109, 3 figs.

In the past 5 years a very large number of chemicals have been tested for insect repellent properties by the U.S. Department of Agriculture Research Service. In recent sorting tests, the compound diethyltoluamide showed promise (*J. Econom. Entom.*, 1955, v. 48, 67, 499, 741; 1957, v. 50, 46). The present paper describes extensive trials with this compound in comparison with established repellents (such as mixtures of DMP, ethyl hexanediol and indalone).

The first tests were in the application of repellents to skin. Some trials were made with caged mosquitoes (*Aedes aegypti*, *Aedes taeniorhynchus* and *Anopheles quadrimaculatus*); others were conducted in the field against wild populations of *Mansonia perturbans*, *Stomoxys calcitrans*, *Chrysops atlantica* and *Culicoides canithorax*. In addition to ordinary protection tests, the effect of wiping and rinsing of skin treated with various repellents was investigated; also the deleterious effect, on repellents, of sweating. In all these tests, the compound diethyltoluamide, and mixtures containing it, compared well with standard repellents and a few other selected new compounds. Generally it was 1.5 to 3 times as effective. The technical grade of diethyltoluamide, which contains about 70% of the *meta* isomer of this compound, was better than samples in which the *ortho* isomer was artificially increased.

Other tests were made with repellents applied to garments. The diethyltoluamide treatment was more effective than a standard mixture against *Aedes aegypti*, about equal against *Aedes taeniorhynchus*, more effective against *Xenopsylla cheopis*, but less effective against *Amblyomma americanum*. Against *Trombicula splendens*, diethyltoluamide and some mixtures containing it, were more effective and persistent than the standard, though less resistant to rinsing. (The standard clothing application contained *N*-butylacetanilide, 2-butyl-2-ethyl-1,3-propanediol and benzyl benzoate.)

J. R. Busvine

GILBERT, I. H. **Evaluation of Repellents against Mosquitoes and Deer Flies in Oregon.** *J. Econom. Entom.* 1957, Feb., v. 50, No. 1, 46-8.

Field studies with repellents have been conducted in Oregon against mixed populations of mosquitoes breeding in snow water, principally *Aedes communis*; against mixed populations of mosquitoes breeding in irrigation water, principally *Aedes dorsalis*; and against deer flies, *Chrysops discalis*. Tests were made with repellents applied to the skin and also to clothing.

As skin application 1 ml. of an ethanol solution of the repellent was applied to the forearm from the wrist to the elbow, and the arm was exposed to "natural infestations" of insects. The criteria of infestation were landings in the case of deer flies and bites in the case of mosquitoes. Each repellent was paired against each other repellent. Against all species of mosquitoes, diethyltoluamide was the most effective of 12 individual repellents tested. It was about twice as effective as the standard, M-2020 containing dimethyl phthalate (40%), dimethyl carbate (30%) and ethyl hexanediol (30%). Against *A. dorsalis* the *ortho* and *meta* isomers of N,N-diethyltoluamide were 45% more effective than M-2020, whereas the *para* isomer was 16% less effective.

The effectiveness of 6 new repellent mixtures was compared with the standard M-2020. Each mixture was paired against each other. It was found that all the new mixtures caused longer protection time than the standard against all the species of mosquitoes. These differences were not as pronounced against *dorsalis* as against the snow-water mosquitoes. The mixtures that contained diethyltoluamide were more effective than those that did not. Against *Chrysops discalis* none of the repellents differed very markedly from the standard in repellency. Applied to the skin, diethyltoluamide was equally as effective as an ethanol solution as it was in pressurized sprays.

Acetone solutions of individual repellents and mixtures of repellents were applied to stockings and shirts and their effectiveness studied after ageing. Almost all the formulations showed complete protection from mosquitoes after 26 days of ageing. They were, however, all ineffective after two rinses in water.

W. Z. Coker

SACCÀ, G. & BENETTI, M. P. Fattori ambientali e fisiologici della inseminazione in *Musca domestica* L. e nelle sue sottospecie. [**Environmental and Physiological Factors in the Fertilization of *Musca domestica* and Subspecies**] *Riv. di Parassit.* Rome. 1957, Apr., v. 18, No. 2, 103-12. [10 refs.] English summary (9 lines).

There are a number of different forms of *Musca domestica* of which the exact systematic status (variety or sub-species) is uncertain. Anatomical differences are rather variable and are generally limited to

the males. The authors describe tests of physiological differences on various strains of 3 of these forms, in regard to fertilization. The forms used were: (1) *M. domestica domestica* (a strain from Switzerland and 1 from Italy); (2) *M. domestica cuthbertsoni* (3 strains from Tanganyika and 2 from Rhodesia); (3) *M. domestica curviforceps* (1 strain from Tanganyika and 1 from Rhodesia). The last is a new sub-species recently described by SACCÀ and RIVOSÈCCHI (*Rend. Acc. Naz. Lincei*, 1955, Ser. 8, 19).

The effects of various factors on fertilization were determined by confining together groups of virgin male and female flies for 24 hours and then dissecting the females to examine the spermathecae. Results were as follows:

Factor	Effect on fertilization in different forms		
	<i>domestica</i>	<i>cuthbertsoni</i>	<i>curviforceps</i>
Age of maturity (days)	<3	3 to 20	3-5
Light	little effect	inhibition in dark	little effect
Small space (25 ml. beaker)	little effect	inhibition in confinement	little effect
Low temperature:—			
Appreciable reduction at:	18°C.	24°C.	18°C.
6% or less fertilization at:	14°C.	18-20°C.	16°C.

The inhibition caused by darkness or confined space was most noticeable in newly started colonies of *M. d. cuthbertsoni*. After several generations in captivity both effects were less pronounced. J. R. Busvine

MENN, J. J., BENJAMINI, E. & HOSKINS, W. M. **The Effects of Temperature and Stage of Life Cycle upon the Toxicity and Metabolism of DDT in the House Fly.** *J. Econom. Entom.* 1957, Feb., v. 50, No. 1, 67-74, 2 figs. [25 refs.]

Some workers believe that the metabolism of DDT into DDE is a major factor in DDT-resistance in house-flies and other insect species. Others have felt that the metabolic changes occur more extensively in resistant insects because these live longer after exposure. Still others conclude, from data showing little dehydrochlorination in resistant flies treated with very large doses of DDT, that the cause of resistance is unknown. The object of this work was to throw more light upon this important question. The metabolism of DDT and the retention of unchanged DDT have been studied quantitatively in larvae and adults of two strains of *Musca domestica*, one susceptible and the other resistant.

It was found that in neither larval nor adult stage was an equal amount of absorbed DDT metabolized by the different house-fly strains. In the resistant strain there were lower amounts of unchanged DDT in the larvae, pupae and adults, resulting from exposure to 25 p.p.m. DDT

in the diet. This finding was attributed as the result of greater metabolism in the resistant strain. This conclusion is reinforced by the fact that the sum of unchanged DDT plus DDE was practically the same at each stage for the two strains, an indication also that DDE is the only metabolite formed in appreciable quantities.

The mortalities of susceptible and resistant female flies after exposure to DDT in small vials were studied at 4 temperatures. The results showed that the susceptible flies were more imperilled by exposure to DDT during comparatively short periods at lower temperatures, such as those that may occur during the hours of night, than were the resistant flies.

Tests were made to determine the effect of temperature upon the absorption of DDT and production of DDE after the exposure of adult flies to a constant amount of DDT. It was shown that with the two strains of flies the absorbed DDT metabolized was: at 1 hour, susceptible (S) 3.6%, resistant (R) 48%; at 2 hours, (S) 15%, (R) 67%; at 4 hours, (S) 23%, (R) 74%; all at 35°C. The high percentages in the case of the resistant flies indicate that metabolism is not too slow to have an effect on mortality.

W. Z. Coker

ASCHER, K. R. S., with the technical assistance of D. ROCH. **Houseflies in Israel—I. A Resistance Survey in Rural Areas.** *Riv. di Parassit.* Rome. 1957, Apr., v. 18, No. 2, 113-22, 5 figs. [18 refs.]

Collections of house-fly larvae were made at over 40 sites in various parts of Israel. From adults which developed from them, eggs were obtained and an F_1 generation reared on artificial medium. The adults of these broods were tested for insecticide resistance by exposing them to insecticide residues (from acetone solutions) in glass bottles, for 10-minute exposures. Resistance was calculated from the ratio of the 50% lethal deposit rate to that obtained with a susceptible laboratory colony. Results showed varying degrees of resistance to DDT and gamma BHC in different parts of Israel (levels from $\times 1.4$ to $\gg \times 28$). There was no evident relation to geographical location, nor a correlation between DDT- and BHC-resistance.

The author claims that his method of measuring resistance is more relevant to field conditions than the topical application test. He considers that resistance levels as low as $\times 3$ may render control difficult.

J. R. Busvine

GRATZ, N. G., ROSEN, P. & ASCHER, K. R. S. **Houseflies in Israel—II. A Preliminary Survey of Species breeding in Rural Areas.** *Riv. di Parassit.* Rome. 1957, Apr., v. 18, No. 2, 123-7.

To obtain house-flies for the resistance tests described in the previous paper [above], collections of fly larvae at various breeding sites were

made throughout Israel. The sites comprised: 27 from cow manure piles, 6 from garbage dumps, 3 from garbage and manure mixed, 2 from chicken manure and 1 from a compost pile. The various flies which emerged were identified and classified.

The flies were mainly *Musca*, of the following species: *domestica domestica*, *domestica vicina*, *domestica nebulo*, *sorbens*, *vitripennis*, *albina*, *lucidula*, *tempestiva*, *crassirostris*, *autumnalis* and *larvipara*. Particular attention was given to separation of *nebulo* and *vicina*. The former, a hot country variety, ranged from 0 to 31% (average 10.8%) of the *domestica* forms, the highest proportions being from South Israel. *Musca sorbens* was rare in Israel as compared with Egypt and this was accounted for by the absence of human stools round the villages, random defaecation being uncommon in rural Israel. [The question is a little "begged" since the survey was made on specimens from selected larval sites. However, the statement may well be true.] J. R. Busvine

KANO, R. & MORIKAWA, T. **Notes on Flies of Medical Importance in Japan. Part XII. Finding of *Calliphora vicina* Robineau-Desvoidy, 1830 in Hokkaido, Japan.** *Bull. Tokyo Med. & Dental Univ.* 1957, Mar., v. 4, No. 1, 69-72, 17 figs.

LECLERCQ, M. Révision systématique et biogéographique des *Tabanidae* (Dipt.) de France. I. [**Systematic and Geographical Revision of the *Tabanidae* of France**] *Ann. Parasit. Humaine et Comparée.* 1957, Apr.-June, v. 32, No. 3, 303-27.

RHODES-JONES, R. **Intestinal Myiasis in Tanganyika.** *J. Trop. Med. & Hyg.* 1957, July, v. 60, No. 7, 169.

Active fly larvae were found during a period of 10 days in the routine examination of stools from 7 African babies in Mwanza, Tanganyika. The larvae were 2-3 mm. in length and a dirty white colour. The infants had had diarrhoea. In 2 cases, flies were reared from the stools and were identified as *Megasilia*. The species was closely related to *M. scalaris* which has often been found in human and animal excreta and has been associated with "several apparently authentic instances of intestinal myiasis".

The fly lays eggs on a variety of substances including rotting fruits. The present cases occurred at the height of the mango season. 2 cases in the literature have been quoted, but this seems to be the first report of myiasis due to *Megasilia* in Tanganyika. H. J. O'D. Burke-Gaffney

FELDMAN-MUHSAM, B. **Revision of the Genus *Hyalomma*. II. The Subgenus *Hyalommina*.** *Parasitology.* 1957, June, v. 47, Nos. 1/2, 46-59, 11 figs. [13 refs.]

AUDY, J. R. **Malayan Trombiculid Mites. 2. Naked-Eye Observations on Attached Chiggers, with a Simple Checklist of Malayan Species, and Details of Preferred Hosts.** Reprinted from *Bull. Raffles Museum*. Singapore. 1956, Dec., No. 28, 86-101, 2 figs. [19 refs.]

This very useful paper gives in tabular form, besides text elaboration and introductory matter, the names of the 83 confirmed species of larval trombiculids collected in Malaya, mainly Selangor, since 1948 by the author and his colleagues. The table gives the size, colour, shape and other features which are of value in identification by the naked eye or hand-lens, and provides facts on hosts and sites of attachment thereon. The figures are line-drawings of views or sections of the head of *Rattus* showing sites of attachment on the chin, cheek, and intranasal passages of certain species or groups of trombiculid larvae. *D. S. Bertram*

See also p. 1168, AUDY, **Trombiculid Mites infesting Birds, Reptiles, and Arthropods in Malaya, with a Taxonomic Revision, and Descriptions of a New Genus, Two New Subgenera, and Six New Species.**

MILANI, R. Errori genetici in ricerche sulla ereditarietà della resistenza agli insetticidi. [**Genetical Errors in Research on Eradication of Insecticide Resistance**] *Riv. di Parassit.* Rome. 1957, Apr., v. 18, No. 2, 129-32.

The author points out that much of the investigation of inheritance of insecticide-resistance has been done by entomologists rather than professional geneticists. As might be expected, quite a number of errors and misunderstandings of genetical theory and terminology have slipped into various papers. Examples are given.

FRYER, S. H. **The Design, Development and Testing of an Insecticide Hand Duster.** *Bull. World Health Organization*. Geneva. 1957, v. 16, No. 1, 227-38, 3 figs.

A convenient insecticide hand duster has been designed for the purpose of de-lousing people, blankets and bedding. It is convenient in that it is small and light, robust, can be operated by hand or by compressed air, and can discharge a constant rate of powder when operated at any angle in the vertical plane.

The duster is constructed of tinned plate and weighs only 4 lb. 3 oz. when charged with 14 oz. of anti-louse powder. It is 26.5 in. long, 5.75 in. wide and 5 in. high. It comprises a dust reservoir, an air-pump, and a discharge tube. Air from the pump enters the dust reservoir from below and blows the dust through the discharge tube. The duster should be used with the top part uppermost.

Attention is drawn to the fact that it is essential to leave the inside of the duster free from insecticide after use. This may be achieved by pumping air through the system. *W. Z. Coker*

KNIFE, F. W. **Pressure Regulators and Gauges on Hand-Compression Insecticide Sprayers: Some Causes of Failure and Suggestions for Improvement.** *Bull. World Health Organization*. Geneva. 1957, v. 16, No. 1, 217-25, 2 figs.

The pressure gauge indicates the pressure developed within the tank and the regulator functions automatically to control and maintain uniform pressure on the nozzle tip. These gadgets are undoubtedly the most delicate accessories used with hand compression insecticide sprayers and, properly maintained, they are worth while.

Fouling of the pressure gauge is often caused by the slow depositing of the insecticide in fairly inaccessible places, *e.g.*, shank stem and perhaps in the U-tube, where it hardens, dries and cannot be removed by ordinary rinsing. Daily cleaning will, however, prevent complete blockage of the passages. It is advisable to have a large orifice through which drainage occurs as this does not block easily. The orifice should be smooth, and where it joins the U-chamber there must be no projections or pockets of any sort as these may trap the insecticide suspensions and start a calcareous deposit.

The gauge should be placed on the sprayer so that the hollow shank and the whole of the U-chamber can continuously drain into the tank. It is not advisable to have gauges whose U-chambers lie in the horizontal plane of the sprayer. *W. Z. Coker*

GOODWIN-BAILEY, K. F., HOLBORN, J. M. & DAVIES, M. **A Technique for the Biological Evaluation of Insecticidal Aerosols.** *Ann. Applied Biol.* 1957, June, v. 45, No. 2, 347-60, 1 pl.

[The use of aerosols for destroying potentially disease-bearing insects in aircraft has become a recognized facet of international quarantine. Thus, all aircraft entering India or Pakistan from Africa must be so treated, to prevent possible introduction of *Aedes aegypti* carrying yellow fever. The World Health Organization specified a formulation for use in solvent-pressurized dispensers, but ends with the words "or any other formulation of equivalent insecticidal activity". It does not say how this shall be determined. The value of the present paper is that it describes a fairly simple workable method of assessing the insecticidal activity of aerosols.]

The tests are done in a small (1,194 cu. ft.) room, painted with white solvent-resistant paint and with the floor covered with clean brown paper. The room is maintained at 80°F. (27°C.) and about 50% relative humidity. The aerosols to be tested are released from their normal

dispensers at the rate of 3 gm. per 1,000 cu. ft. (Dosing is judged by time of release and checked by weighing before and after.) The insecticidal action is assayed by the effect on house-flies, reared under standard conditions. About 400 flies are released from floor level immediately after discharge of the aerosol. The rate of knockdown is measured by counts at 2-minute intervals up to 10 minutes and from these data the time for 50% knockdown is calculated. (This is the main basis of assessment of the insecticidal action.) The flies are all collected after 10 minutes and kept in clean containers for 24 hours. Any effective treatment must give 100% kill.

The authors report tests in the same room with the flies confined in 4 1-ft. cube cages fixed to the walls. The results with the caged flies were considered to be more erratic than with free flying flies and also less comparable with results obtained under practical conditions.

J. R. Busvine

See also p. 1261, COLONIAL OFFICE. **Colonial Pesticides Research Committee. 9th Annual Report, 1955-56.**

MISCELLANEOUS PAPERS

MANUWA, S. L. A. **Notes on the Estimation of Age of Nigerian Children.**

West African Med. J. 1957, June, v. 6 (n.s.), No. 2, 58-63, 4 graphs & 1 diagram.

These notes have been prepared by the Chief Medical Adviser to the Federal Government of Nigeria for the guidance of Medical Officers in assessing the age of Nigerian children. They are based on a memorandum written by a former Senior Pathologist and have been amplified and revised in consultation with a number of experts in the Federal Medical Services.

Sir Samuel begins by pointing out that since there are various tribal, social, environmental and other variations in the bodily development of Nigerian children, estimation of their age can never be completely accurate. However, he puts forward the following 7 criteria which when combined should enable an examiner to make a reasonable estimate of the age of a child.

General appearance is purely a matter of experience, but may be taken into account in the light of the other criteria.

Height and weight may serve to corroborate the general impression. Graphs are presented which show the average heights and weights of Nigerian persons of each sex from 6 to 20 years and the range covered by 75% of the measurement for each yearly group. The heights and weights are read from a vertical scale and the points at which this level cuts the 3 lines of the graph show the average age and upper and lower limits, in so far as only 75% of the values will fall within the limits

shown on the graphs. Furthermore, certain tribes are taller than others and there are also variations according to social factors.

Hair development is on the whole less marked in Africans than in Europeans. Pubic and axillary hair is not usually present at the age of 12, but a scant growth is often visible at 14. If this hair is fully developed, the age is greater than 14. A vigorous beard in young men rarely occurs before 18.

Deepening of the voice occurs about 14 and has usually deepened to adult tone by about 18.

Development of teeth may be a very useful criterion, especially that of the 2nd and 3rd molars. Supernumerary teeth may be misleading, but they are always smaller than normal and peg-shaped. The 1st permanent molar erupts fairly consistently between 5 and 7 years, and the 2nd at about 12; if none of these are present, the child is almost certainly less than 12. If all 4 of the 2nd molars are present, but not the 3rd, he is between 12 and 15. The eruption of the 3rd molar is variable, but in general it does not appear in Africans before the age of 15. If 3 or 4 of these teeth are visible, the person is almost certainly 18 or more [see also this *Bulletin*, 1948, v. 45, 125 for findings in East Africans].

Radiological examination of bones is not likely to add to the information gained from the other criteria. The author refers to the studies of MACKAY [*ibid.*, 1952, v. 49, 658] on the maturation of the carpal bones in East African children and also quotes some American figures relating to the elbow bone. It would seem that the bone maturation of Africans occurs about 2 years later than that of the white races; but, again, these data are only approximate.

The age of onset of menstruation is discussed on the basis of the study of Nigerian girls carried out by ELLIS [*Bull. Hyg.*, 1951, v. 26, 12].

Sir Samuel ends his notes by inviting comments on them by Medical Officers in the light of their experience in the use of them.

[Those who are constantly faced with the difficult problem of assessing the age of Africans for medico-legal purposes will welcome these constructive notes.]

H. J. O'D. Burke-Gaffney

REPORTS AND SURVEYS

COLONIAL OFFICE. **Colonial Research 1955-1956. Colonial Medical Research Committee. Eleventh Annual Report (1955-1956)** [HIMSWORTH, H. P., Chairman] (pp. 135-80). Cmd. 52. 312 pp. 1956, Nov. London: H.M. Stationery Office. [10s.]

This is a committee of the Colonial Research Council, and it is served by sub-committees on malaria, helminthiasis, personnel, and leprosy

(including a laboratory panel), and an advisory working-party on the sickle-cell trait and sickle-cell anaemia. The present report, like its predecessors, describes the work done in the year by the committee and by the many regional organizations and individual workers throughout the British overseas territories who are financed wholly or partly by the committee. The account is set out first under the headings of disease groups, and then under the headings of the institutes in West and East Africa, and miscellaneous projects. But, as before, there is a section—short but by no means negligible—on research undertaken and financed by the medical departments of the territories themselves.

Filariasis has received much attention. In the Cameroons the study of *Loa loa* and its vectors, and of the form found naturally in forest monkeys (which exhibits nocturnal periodicity), has been continued under the supervision of the Liverpool School of Tropical Medicine. In East Africa an attempt is being made to eradicate *Wuchereria bancrofti* from an island in Lake Victoria by administration of diethylcarbamazine. In Malaya the exciting discovery in monkeys, dogs and cats, of microfilariae very closely resembling those of *W. malayi*, and of one type of adult also very close to *W. malayi*, is being developed. Whatever may prove to be the relationship of these to the human filaria, their presence confuses the interpretation of dissections of wild-caught mosquitoes.

Work on the snail hosts of schistosomes proceeds in West Africa, and on guinea-worm in Nigeria.

In East Africa preliminary investigations on the populations of the vectors of malaria have been made. They will provide a standard of comparison for surveys made after the projected extensive house-spraying campaign has been started in the Pare area. In Nigeria the large control project in Western Sokoto, now in its second year, and organized jointly by WHO, the Government, UNICEF and the present committee, has met the problem of resistance to insecticides by *Anopheles gambiae*, and this forbidding problem is receiving serious attention. A long-term experiment in prophylaxis with pyrimethamine in Gambian children indicates that the drug reduces the death rate in the first 16 months of life and prevents early anaemia and deficiency of weight, but that by 161 weeks there is not much difference between children taking the drug and control children. Breast milk offers little protection against malaria in Gambian infants.

In Nigeria yellow fever is being investigated, and discrepancy has been found between the results of mouse-protection tests and haemagglutination-inhibition tests. It seems probable that other viruses (for instance Uganda S, Zika, and West Nile) may be serologically related to the yellow fever virus, and confuse the picture presented by human antibody surveys.

In East Africa the Rift Valley fever virus has been studied, and a new Group A virus, closely related to Semliki Forest virus, has been identified from the large epidemic of dengue-like disease.

In Trinidad the staff of a laboratory financed jointly by the Government and the Rockefeller Foundation report high immunity rates to Ilheus virus, and the isolation of this virus from mosquitoes and from one patient with severe encephalitis. The outbreak of yellow fever which began in 1954 apparently ended about January 1955, when the virus was isolated, for the last time, from the liver of a dead howler monkey. A new virus, Mayaro virus, was isolated from a patient in 1954, and several other unidentified viruses have also been isolated from patients, and many from mosquitoes.

In Malaya evidence accumulates which shows that Japanese encephalitis virus is widely, but unevenly, spread in man, and that it chiefly causes disease in domestic animals. Leptospire are found in many forest rats which do not show agglutination-lysis antibodies, and this important finding is being followed up. Leptospirosis, dengue, malaria and scrub typhus continue to be the most common causes of pyrexia in and around Kuala Lumpur.

In East Africa 3 forms of *Ornithodoros moubata* have been distinguished, which feed on man, chicken and wart-hog respectively. The blood meals of tsetse flies have again been studied by the haemagglutination-inhibition technique.

Physiological and nutritional researches were carried out in East Africa, where studies were made of diets and serum proteins and lipids. In Nigeria the effects of air movement and climatic conditions on reactions to heat and on performance of skilled tasks showed that there was some diminution in efficiency during a succession of tests in the heat. Detailed physiological observations are reported from the Tropical Metabolism Research Unit, Jamaica, where malnutrition is a major subject of study.

The sickle-cell trait has received much attention, particularly in relation to the chemistry of haemoglobin and the conditions of deoxygenation in which sickling occurs; most sickle-cell homozygotes, and most persons with haemoglobins S and C, die before reaching adult life.

Work on the treatment of leprosy continues, and a new drug—diphenyl thiourea—gave promising results in Nigeria.

In Gambia it has been shown that even small doses of diethylcarbamazine may sterilize mature *W. bancrofti* and terminate the production of embryos; small doses repeated at long intervals may therefore eventually reduce the microfilarial reservoir without causing the severe reactions seen when large doses are given.

The East African Medical Survey and Research Institute continued to make observations on the local populations, especially schoolchildren.

Research undertaken by the medical departments of the countries themselves includes therapeutic trials in malaria in Malaya, and the study of anaemia there, and in Kenya the investigation of the vectors of kala azar. In Fiji various vectors of *W. bancrofti* were incriminated—*Aedes pseudoscutellaris*, *polynesiensis* and *fijiensis*, and *Culex fatigans*.

Monthly administration of diethylcarbamazine seems to be valuable in reducing the number of carriers of *W. bancrofti*. Charles Wilcocks

COLONIAL OFFICE. **Colonial Research 1955-1956. Colonial Pesticides Research Committee. Ninth Annual Report (1955-1956)** [HALL, W. J., Chairman] (pp. 181-207). Cmd. 52. 312 pp. 1956, Nov. London: H.M. Stationery Office. [10s.]

The Colonial Pesticides Research Committee is the new name for the former Colonial Insecticides, Fungicides and Herbicides Committee.

The present report indicates briefly the progress of work at Porton on the sorption of insecticides by soils and the behaviour of urea-formaldehyde resin films, with special attention to the influence of humidity and temperature; also residual activity of DDT and dieldrin on vegetation; insecticide formulations; cumulative effects of sub-lethal doses of several insecticides; and matters concerning spraying from aircraft.

Research at Silwood Park laboratories and at Rothamsted Experimental Station covers the contamination and penetration of various insects by DDT, olfactory function in tsetse flies, and factors affecting the persistence of DDT films in sunlight and on plant leaves.

A brief account is given of several schemes of work with tsetse fly and mosquitoes in East Africa. A Biting Fly Research Unit is now active in Uganda; it is doing general surveys in the field and has established a successful laboratory culture of *Stomoxys calcitrans*. Control of *Simulium neavei* by DDT-treatment of rivers in an onchocerciasis area in the West Nile district of Uganda is reported. From West Africa there is detail, based on chemical analysis, of the fate of DDT, BHC and dieldrin on sprayed mud surfaces in the Malaria Control Pilot Project in Sokoto, Nigeria. Researches in filariasis in Fiji are outlined.

D. S. Bertram

EAST AFRICA HIGH COMMISSION. **East African Trypanosomiasis Research Organization. Annual Report 1955-56** [FORD, J., Director]. 50 pp., 3 figs. on 2 pls. [15 refs.] 1956. Nairobi. [Shs. 7/50.]

Introducing this report, which covers the period between 1st July 1955 and 30th June 1956, the Director (Mr. J. Ford) records the accomplishment of the reorganization projected in the previous annual report [see this *Bulletin*, 1956, v. 53, 942], and describes briefly the staff position and accommodation. In a short summary of the work of the Organization he emphasizes the linking of their research with the practical problems of trypanosomiasis which need solution for the proper development of East Africa. He points out that the chief value of the new techniques evolved is that they permit the productivity of areas under reclamation to be raised far more quickly than in the past. He describes

also how research on trypanosomes, which has so far lagged behind that on tsetse, is being accelerated to reduce this lack of balance; two important problems under investigation are the production of simple reliable field tests for trypanosome infections and the extremely complex one of "trypanosome challenge". Gratifying evidence is given of ever strengthening collaboration with other departments.

Under Tsetse Research the Chief Entomologist (Dr. J. P. GLASGOW) discusses the latest evidence regarding the long-term cycle of tsetse numbers, the development of the work on the food of tsetse [see also *ibid.*, 1957, v. 54, 657] and of the study of the natural resting sites of tsetse which have been found between 3 and 15 feet above the ground; this study also emphasizes the sparsity of tsetse [though his figure of 1 female per 10 square yards should, the abstracter understands, be 1 per 10 yards square]. On the laboratory side he mentions work on the behaviour of tsetse in relation to humidity, which may eventually illuminate field studies by the suggestion that tsetse can to some extent create their own microclimate [it is to be hoped that the further studies needed to confirm this will be carried out]. Research on the sense organs such as that which located, in the flagellum of the antenna, the sensilla which guide the fly in its choice between higher and lower humidities is obviously an essential foundation for behaviour studies, as is also the work on pupal respiration and water regulation which showed that, when kept under identical conditions, *G. morsitans*, *G. swynnertoni* and *G. pallidipes*—species living in drier habitats—lose less water than *G. austeni*, *G. palpalis* and *G. brevipalpis*—species restricted to moister situations. The problem of the satisfactory maintenance of tsetse in the laboratory still awaits solution, though what may prove an important contribution to this is the discovery that unless frequent change is made of the animals on which the tsetse are fed, the reproductive capacity of the flies decline; this may also bear on the study of population dynamics, since it suggests the possibility of a limit to the number of tsetse supported by one animal, so that food supply, previously considered not to be a limiting factor, may turn out to be one. The use of ultra-violet light led to no improvement in methods of catching flies, but traps not only raised the numbers of females caught but are also elucidating the variation in composition of the catch at different times of day, as well as aiding in the study of dispersal of flies. The virtual abolition of human trypanosomiasis and better prospects for the introduction of cattle are described as resulting from discriminative clearing directed against *G. morsitans* at Urambo. The investigation of methods of bush clearing, with emphasis on the suppression of regeneration, is also reported.

Under Trypanosomiasis Research, the Senior Medical Research Officer, Dr. K. C. WILLETT, records a year of continuous expansion with near attainment of full strength. Details of the animals maintained give one an idea of the scale on which work is carried out. He distinguishes between the routine maintenance of strains for short-period investigations

and that for longer periods for use as standards, and notes the large numbers of the former maintained this year, mainly for work in cooperation with other departments. He comments on the immense help that reliable maintenance of strains by means other than transmission from animal to animal would be, and mentions preliminary experiments on the storage of strains in deep freeze or in freeze-dried condition; full prosecution of these, however, awaits the arrival of better equipment.

Under Protozoological Research, work carried out with Professor R. M. GORDON of the Liverpool School of Tropical Medicine is described; this indicates that there is no direct cycle of the trypanosome in the mammal comparable with the pre-erythrocytic cycle of malaria, though it does not completely exclude such a possibility. An investigation of the phenomena of polymorphism, originated by another visitor—Dr. D. WIJERS from the School of Tropical Medicine in Amsterdam—is now being extended by members of EATRO staff. Studies of the factors concerned in the infection of the tsetse with trypanosomes indicate that crithidial development takes place somewhere between the proventriculus and the salivary glands. Subsequent feeding of infected tsetse on blood of baboons (an animal which it has been impossible to infect with trypanosomes) was found not to affect the final infection rates of the flies; this is important for it shows that by using baboons for subsequent feeding infection rates can be studied with the assurance that the only infecting feed will have been the first one. The Tinde strain of *T. rhodesiense* was still infective to man after 21 years of transmission through sheep by *G. morsitans*. An investigation of the effect of cortisone on infection by *T. rhodesiense* of white rats suggests that this is of two kinds—a lowering of the acquired immunity of the host, and an inhibitory effect on the trypanosome. The first tends to enhance the parasitaemia while the second has an opposite effect either by production of an antihormone or more likely by creation of an environment adverse for the trypanosome. Thus the time of administration affects the results; administration just before an infecting dose may so affect the defence mechanism that the inhibitory effect on the trypanosome is outweighed, whereas if the drug is given during the course of an infection, with immunity already developed, the effect on the trypanosomes may be enhanced. These results also throw doubt on the value of this drug in diagnosis to bring out latent infection.

Under Epidemiological Research, a survey of the tsetse and the trypanosomes they carry on the Samia-East-Busoga border has shown a difference in infection rate between two species of tsetse, *G. pallidipes* and *G. palpalis fuscipes*, which is a reflection of the different hosts used by the two species, the infection rates also being related to season, possibly through its effect on the length of life of the fly, and to habitat. In cooperation with the Kenya Government's survey of sleeping sickness in Central Nyanza, where an infection originally of the Gambian type has been replaced by one of the Rhodesian type, 10 strains of polymorphic trypanosomes have so far been isolated from the possible vectors (*G.*

palpalis fuscipes 3, and *G. pallidipes* 7); these are being investigated as to virulence to small laboratory animals, frequency of posterior-nuclear forms, and arsenical resistance and infectivity to man (at Tinde); so far, all the 7 strains at present under test for the last character have been negative and must therefore be regarded as *T. brucei*. Another line of epidemiological research is an investigation of the history of the introduction of human sleeping sickness into Uganda and an attempt to link this with an ecological study of the man-fly contact, with the use of traps as the means of sampling the fly. A specialist unit for the study and treatment of sleeping sickness has been established at the laboratory itself.

Biochemical Studies have included the demonstration of a small difference in oxygen metabolism between strains passaged by cyclically infected tsetse flies and by syringe; such differences, it is suggested, might be used to distinguish between *T. rhodesiense* and *T. brucei*. Attempts at culture of trypanosomes in the laboratory, mainly as a means of investigating the fundamental metabolic requirements of the trypanosomes, have resulted in maintenance of growth and multiplication up to 72 hours, and survival without multiplication for 120 hours.

Under Immunology and Diagnosis, continuation of the experiment on immunity in cattle after a period of exposure to trypanosome infection while protected with Antrycide showed no trypanosomes in the various groups of treated animals, except for a single beast in the group given 7 eight-weekly doses of Antrycide pro-salt and *T. congolense*; the animals of the untreated groups all died with typical symptoms of the disease after an average period of 120 days. A field experiment at Kiboko on acquired immunity under Antrycide protection has been closed down after it had shown no appreciable acquired immunity in any of the cattle, which had received two-monthly doses of Antrycide either for 6 months, or for a year with and without the additional challenge of infected blood. Attempts to find a reliable method of enumerating trypanosomes, simpler and easier to carry out than the haemocytometer method, have so far failed; counts by a thick smear technique did not agree with parallel counts by the haemocytometer. Preliminary investigation on the size of minimal infective dose has shown striking differences between strains and species.

Under Chemotherapy, all the trypanosome strains obtained in the epidemiological work described, or from patients under study for sleeping sickness, are tested for resistance to tryparsamide and some also against pentamidine. 3 new drugs—the antibiotic Stylomycin, a new product of Imperial Chemical Pharmaceuticals and a Boots product for use as a prophylactic against cattle trypanosomiasis—are being investigated in cooperation with the interested territorial departments.

Under Reclamation, progress in the winding up of the Pilot Schemes for reclamation is reported. The replacement of that sited in Kenya by a new scheme operated by the Veterinary Department of that Territory was reported last year [see *ibid.*, 1956, v. 53, 942]; that in Uganda is to

be expanded under the direction of the Uganda Tsetse Control Department with the object of eventually eliminating *G. morsitans* from nearly the whole of Ankole; observational work on this will be continued by EATRO until the fate of the tsetse in all the areas treated is determined; tsetse cannot now be found in much of the area treated in 1952. An advance which occurred during the operations had already necessitated the extension of the scheme over an area of 600 square miles instead of the 250 originally planned. A full description of the work by the officer concerned is given; the cost of the discriminative clearing varied between just over 1 man-day per acre to as much as $5\frac{1}{2}$, the differences being partly due to the type of country treated and partly to improvements in technique; the area actually cleared was only a tenth of that originally occupied by the fly, and this reduced the cost of the land freed proportionately. Mechanical clearing was found to be, at its cheapest, about half as expensive again as hand clearing and at its dearest 6 times as much; the cost of its use against trees of over 10 inches in diameter was prohibitive. It is, however, thought that with different machines the costs can in future be reduced, whereas those of hand labour will certainly rise. It is concluded that the primary object of the scheme, the evolution of a technique of discriminative clearing to eliminate *G. morsitans*, has been achieved in a way that makes the reclamation of extensive areas practicable.

The Tanganyika scheme—the creation of a tsetse-free area for the wet-season grazing of cattle in the middle of a fly belt—has also been completed, by the linking with clearings of “mbuga” systems to form a mile-wide cleared barrier round the 40 square miles of grazing which constitute the area, and by the selective clearing of riverine forest, inside the barrier clearing, against 3 species of tsetse (*G. pallidipes*, *G. austeni* and *G. brevipalpis*), and of savanna woodland in a zone 2 miles wide, outside, against *G. morsitans*. This is fully reported by the officer concerned, but most of the data on the fly remain to be worked out. The cost of the riverine clearing was provisionally 15 man-days per acre as a general average, to which the cost of burning [to check regeneration] would have to be added. Satisfactory reduction in fly numbers is recorded. Probably less than half the time spent by teams using mechanical saws (in their second year) was actually occupied in felling trees, and it is suggested that more robust saws would give better results though their weight would have to remain within the capacity of 2 African operators.

The list of publications shows 14 scientific papers actually published during the year, and 7 more accepted for publication. The Staff List shows a Director and Secretary and 2 others on the administrative side, with the post of Deputy Director still vacant; at the Central Tsetse Research Laboratory are 7 technical officers, 2 field officers, a secretary and a mechanic (no vacancies), and in the Trypanosomiasis section 9 technical officers with 4 laboratory technicians and a field assistant (no

vacancies, but 3 not yet arrived); under Experimental Reclamation were 2 technical officers, 3 field officers and a field assistant.

This imposing record of achievement should be studied in the original by all interested in the problems of trypanosomiasis. *W. H. Potts*

- i. PAVLOVSKY, E. N., PETRISHCHEVA, P. A., ZASUKHIN, D. N. & OLSUFIEV, N. G. [Edited by.] **Natural Nidi of Human Diseases and Regional Epidemiology. Proceedings of the Joint Conference of the USSR Ministry of Public Health, the USSR Academy of Medical Sciences, the Gamaleia Institute of Epidemiology and Microbiology of the USSR Academy of Medical Sciences, dedicated to the Seventieth Anniversary of E. N. Pavlovsky, Memb. USSR Ac. Sci. March 29–April 1, 1954.** 532 pp., numerous illustrations. [Numerous refs.] [In Russian.] English summary. 1955. Leningrad: State Publishing House of Medical Literature Medgis.
- ii. BLÁŠKOVÍČ, D. [Edited by.] *Prirodné Ohniská Nákaz. Sborník prác o prírodnej ohniskovosti rôznych nákaz človeka, zvierat i rastlín v zmysle učenia akademika E.N. Pavlovského.* [**Natural Foci of Infectious Diseases. Symposium on Natural Focalization of Infections in Man, Animals and Plants, according to the Doctrine of Academician E. N. Pavlovsky**] 365 pp., illustrations. [In Czech & Slovakian.] Russian & German summaries. 1956. Bratislava: Slovakian Academy of Sciences.

It has long been known that a number of human diseases transmitted by arthropods and other invertebrate vectors are also shared by wild animals, which act as reservoir hosts from which man may acquire the infection. The best-known examples of such zoonoses are plague, leishmaniasis and trypanosomiasis (Chagas's disease and Rhodesian sleeping sickness). The recognition of the important epidemiological role of zoonoses has led to intensive studies of the ecological conditions under which such infections are maintained among the wild animal hosts and vectors. From the valuable information thus obtained a coherent pattern has emerged which provides a rational basis for the control of the diseases in question.

To the eminent Soviet parasitologist, Academician E. N. PAVLOVSKY, belongs the merit of having integrated the ecological and epidemiological data on zoonoses into a new doctrine of natural focal distribution or "nidality" of transmissible and other infectious diseases. He has shown that they occur within geographical areas, the terrain of which is characterized by well-defined ecological peculiarities, determined by topography, climate, vegetation and other environmental factors. In such natural foci the pathogens, their vectors and vertebrate hosts form an association or biocoenosis, within which the infection circulates independently of man as long as human beings do not come in contact with them, but when

this takes place the infection spreads to man and the wild animals become reservoirs of the disease in question.

Natural foci thus constitute a potential epidemiological danger, and it is important that their existence and localization should be recognized beforehand, so that they can be avoided or brought under control. A knowledge of the geographical background or terrain (Pavlovsky's "landscape epidemiology") of the zoonoses is therefore of the greatest importance in assessing the epidemiological situation of territories about to be occupied by man.

Pavlovsky and his associates have succeeded in detecting and controlling a large number of natural foci of transmissible infections within the Soviet Union [see also this *Bulletin*, 1944, v. 41, 331; 1946, v. 43, 65] and the concept created by him has resulted in fruitful work on these lines in Eastern Europe and Asia. It may be noted that a similar ecological approach to epidemiological problems has also been advocated in other parts of the world [*ibid.*, 1942, v. 39, 834; 1954, v. 51, 859; 1956, v. 53, 732; 1957, v. 54, 232].

The interest in the focal distribution of infectious diseases and the immense amount of investigations and field observations carried out on this subject in the Soviet Union and in Czechoslovakia are reflected in the symposia of papers contributed in 1954 at two conferences, one of which was held in Moscow and the other in Bratislava, at which 70 and 29 papers respectively were read. Within the limited space available for review, it is only possible to give a general account of the scope of these symposia, but fortunately 30 papers of the Russian symposium have been abstracted in *Rev. Applied Entom.*, Ser. B., 1956, v. 44, 145, to which the reader is referred for further information.

i. The Moscow Symposium is introduced by E. N. PAVLOVSKY, who discusses the present state of knowledge regarding natural focal distribution of human diseases, while I. G. GALUZO extends this concept to the diseases of domestic animals, many of which were found to be also prevalent among wild animal reservoirs. A number of papers are devoted to tularaemia: in a study of a focus of the water-meadow type, N. G. OLSUFIEV *et al.* show that it is characterized by the presence of water rats, horse flies and mosquitoes, while V. P. ROMANOVA and other authors have incriminated hamsters, voles and ticks as wild reservoirs and vectors of this disease. T. DUNAEVA describes the course of tularaemia in wild rodents and its bearing on their epidemiological significance. Other communications are devoted to the bionomics of the rodent reservoirs and methods for their destruction.

Among other bacterial infections, observations on natural foci of brucellosis are of particular interest: thus M. M. REMENTZOVA and A. N. GUDOSHNIK established spontaneous infections in a number of different ticks, while S. I. KHARLAMOVICH demonstrated positive reactions to brucellosis in antelopes, rodents, foxes and birds. Natural foci of erysipeloid and listerellosis among wild and domestic rodents, probably

transmitted by Ixodid ticks, are brought to light by M. N. TERESHCHENKO and others. A number of papers deal with rickettsial infections (haemorrhagic fever) and Q fever, and their transmission by mites associated with wild animals. Animal reservoirs of leptospirosis in natural foci are described by V. V. ANANJIN and others, and 2 papers are devoted to the role of wild animals in the dissemination of tick-borne encephalitides.

Among the protozoal infections with a focal distribution, toxoplasmosis, leishmaniasis and pneumocystic disease are described. Other communications deal with malaria, amoebiasis, arthropod vectors of disease, helminthic infections and rodent control.

ii. The Bratislava symposium is devoted to general questions regarding zoonoses and natural foci of diseases of man, domestic animals and plants, and to observations carried out in Czechoslovakia. R. RADVAN reports the finding of a focus of tick-borne encephalitis in Bohemia; V. V. ANANJIN, E. KMETY and V. JELINEK deal with natural foci and reservoirs of human and animal leptospiroses; K. HEYBERGER *et al.* describe a natural focus of tularaemia in Moravia, implicating ticks as vectors and rodents as reservoirs; L. SYRŮČEK and K. RAŠKA believe that Q fever in Czechoslovakia occurs in domestic animals, from which it spreads to human beings; N. G. OLSUFIEV suggests that erysipeloid and listerellosis, occurring in natural foci among various wild rodents, are probably transmitted by ticks, whereas in towns rats and mice serve as reservoirs from which the infection is transmitted by fleas; according to B. RYŠAVY and B. ERHARDOVA, fowl coccidiosis may be acquired from pheasants and partridges, while hares serve as reservoirs of rabbit coccidiosis; similarly it is thought that domestic ruminants may acquire some of these parasites from their wild congeners; V. DYK emphasizes the danger to freshwater fisheries of parasitic infections spreading from fishes of no economic importance; finally, V. VALENTA extends the concept of natural foci to cultivated plants, an example of which is presented by a virus disease of tomatoes (Big Bud or Stolbur) transmitted by a Hemipteran insect; this disease also occurs in various wild plants which serve as reservoir hosts for the cultivated plant.

Most of the papers in the Russian and Czechoslovakian symposia have numerous references, and some are illustrated by figures. C. A. Hoare

ESTÈVE, H. Enquête démographique comparative en pays Fang, district d'Oyem (Gabon) 1952-1955. [**Comparative Demographic Survey of the Fang in the Oyem District of Gabon in 1952-1955**] *Méd. Trop.* Marseilles. 1957, Jan.-Feb., v. 17, No. 1, 85-105, 2 maps. [10 refs.]

The Fang are a tightly knit clan-like subdivision of the Bantu race widely dispersed over western equatorial Africa and constituting one-third of the population of Gabon. The author reports surveys on two groups

in which some demographic measurements were made in 1952 and 1955. One of these groups lives remotely in the bush where communications are still difficult, and the other lives around the headquarters of the district and is much affected by metropolitan influence. The figures here quoted refer to 1955 and in each case the first is that for the peri-urban community and the second for the bush community. The populations are extremely sparse; the proportion aged 10 years or less is abnormally low (21.7%; 23.0%) for such communities, and the population pyramids in some places are partially inverted. The proportion of males to females is low (78.5 and 70.0 per 100) and the number of children aged 14 or less per 100 women (47 and 69) is very small and may be compared with a normal figure of 100 to 130 for such populations. Death rates are high (40.0 and 39.7 per thousand) and include a high infant mortality (229 and 213 per 1,000 births) and the deaths of 55.7% and 44.7% of children before the age of 15. Unmarried women constitute 33.1% and 27.3% of all women, though the proportions without children are smaller, while the average number of past pregnancies in the peri-urban area is 3 per adult woman, and in the bush area, 5.

These figures together give a picture of a population which is regressing rapidly. The causes of the regression are to be sought in social, economic and cultural conditions as well as in disease which manifests itself particularly in the form of yaws, leprosy, malaria, gonorrhoea, tuberculosis and protein malnutrition. Prominent among the adverse factors is the decline of the custom of marriage owing partly to an increasingly burdensome dowry system and partly to a white-collar psychology which sees indignity in the common methods of acquiring the dowry. The report includes a description of the people and their customs in so far as they might be related to these matters.

G. Macdonald

BOOK REVIEWS

WRIGHT, C. A. **A Guide to Molluscan Anatomy for Parasitologists in Africa.** 20 pp., 15 figs. 1957. London: British Museum (Natural History), Cromwell Road, S.W.7. [1s. 6d.]

In recent years much emphasis has been placed on the need for identification in the field of molluscan vectors of schistosomiasis. The unreliability of shell characters alone has led to the need for study of the soft parts of the snail for examination of organs likely to provide characteristic variation sufficient for species separation. This pamphlet fills a much needed want in providing simple instructions for dissection and simple well-illustrated accounts of the structure and arrangement of the digestive and reproductive organs of three essentially different snails,

Lymnaea natalensis, *Bulinus* (*Physopsis*) *globosus* and *Biomphalaria pfeifferi*.

In instructions to the amateur, the author recommends that a collection of the locally common snails should be sent for identification to a malacologist who, in turn, should provide an account of the characters on which his identification is made. In this way, with the aid of a simple dissection technique, the field worker may acquire the ability to make subsequent identifications for himself. The dissecting instruments are simple. Details of several methods of killing, fixation and preservation of snails for dissection are given and, for use where practicable, techniques for narcotization are provided so that the animal may be fixed in an extended condition. The technique of dissection to display the diagnostic characters of the digestive and reproductive systems is broadly the same for all three species and is described clearly, as is the method for removal and preparation of the radula for microscopic examination. Detailed descriptions of the anatomy of each species essential to identification are preceded by a general account of the common anatomical pattern. For each species the description of the anatomy is illustrated by diagrams depicting the general view of the entire and the opened animal and the characteristic appearance of the digestive and reproductive systems as these organs are unravelled. Particular attention is paid to the comparative anatomy of the male reproductive organs since these frequently possess distinct diagnostic characters. All diagrams are adequately labelled with reference to a key.

This pamphlet should prove of great practical value to those who are interested in the identification of molluscan vectors but who hesitate to attempt dissections through lack of elementary information on procedure.

O. D. Standen

BRITISH ENCYCLOPAEDIA OF MEDICAL PRACTICE. **Pharmacopoeia.** 2nd Edition. pp. viii + 696 + 32. 1957. London: Butterworth & Co. (Publishers) Ltd., 88, Kingsway, W.C.2. [65s.]

The Second Edition of the *British Encyclopaedia of Medical Practice* was published in 1953 and one of its volumes was a pharmacopoeia which listed and described a selection of proprietary drugs manufactured in Great Britain. The *Pharmacopoeia 1957* is a new and enlarged edition of this volume, and contains an account of more than 1,400 proprietary preparations. These are arranged alphabetically under their brand names. Each monograph describes the chemistry or composition of the drug, its pharmacology, indications and contra-indications, toxic effects, dosage, method of administration and details of the packings available. Drugs which are controlled by the Poisons Schedules, Dangerous Drugs Act or Therapeutic Substances Act are labelled appropriately. An index

of preparations described in the 1953 edition of the *Pharmacopoeia* but omitted from the present edition is headed "Discontinued Products". It contains a number of drugs which are still widely used, and it is difficult to understand why some of them appear in this list. There is also a list of addresses of pharmaceutical manufacturers in the United Kingdom and overseas, and a "Condition Index" which the publishers have provided to "facilitate reference to the agents which can be used in connexion with various diseases".

Descriptions of the preparations have been supplied by the manufacturers, and are clearly related to the advertising material which they circulate to the medical profession. Claims are in general modest, reasonable and gently persuasive. Enthusiasm occasionally breaks through and pharmacology gives place to "advantages", but absurdities such as "It is unrelated to any other chemical substance" (p. 361) are rare.

In some instances, in order to be fair to the manufacturers, more than one proprietary brand of the same substance has been included, and this makes for a good deal of repetition. Thus $1\frac{1}{2}$ pages of text are devoted to Cortef, 4 pages to Cortril and $2\frac{1}{2}$ pages to Ef-Cortelan; all these are brands of hydrocortisone.

Real difficulties arise with the "Condition Index" and a few examples will indicate its many shortcomings. Suppose that one wishes to prescribe an analgesic. There is no entry for analgesics in the index. Under "Pain", 7 preparations are listed; one of them is morphine (included only because of its trade-name Hyperduric) and the others contain barbiturates, amidopyrin, aspirin, phenacetin and salicylates in various combinations. In order to find a preparation containing codeine it is necessary to refer to the 32 entries under "Neuralgia"; the homely Veganin appears only under the heading of "Sedation".

The book contains monographs for three preparations of piperazine: Antepar, Entacyl and Helmezine. For the treatment of "Ascariasis", Antepar and Hesperidin are listed. Hesperidin is written in error for Hetrazan and this mistake is repeated under "Filariasis", "Onchocerciasis" and "*Loa loa* infestation". Under "*Ascaris lumbricoides* infection" we find Helmezine, Entacyl and Crystoids (hexylresorcinol).

"Threadworms" do not appear in the index. Under "Oxyuriasis" we find Antepar, Plotycin and Nyxolan but not Helmezine or Entacyl. Under "*Enterobius vermicularis* infections" we find Crystoids, Entacyl, Entero-Vioform and Leucarsone, but still no Helmezine. The manufacturers of the product, as well as the prescriber, have grounds for complaint.

The index appears to have been compiled mechanically and not very carefully from the text by a staff with little knowledge of medicine or pharmaceuticals. Perhaps it is significant that the title page of the book acknowledges neither an editor nor a medical adviser.

Substances which appear in the *British Pharmacopoeia* or the *British*

Pharmaceutical Codex are ignored unless they happen to have trade names. There is no sure way of identifying proprietary preparations which contain the same active substance apart from reading the whole of the text.

As a source of information upon the constitution of proprietary medicines this is a valuable reference book. It should be regarded as supplementary to the *British Pharmaceutical Codex*; its title, as a volume in a standard medical encyclopaedia, should have been *Pharmacopoeia of Proprietary Medicines* in order to indicate its scope and limitations. It would benefit greatly from a revision and extension of the "Condition Index" and the addition of an index relating chemical substances to the preparations which contain them.

L. G. Goodwin

NOTICE

SIXTH INTERNATIONAL CONGRESSES ON TROPICAL MEDICINE AND MALARIA

The Sixth International Congresses on Tropical Medicine and Malaria will be held in Lisbon from September 5-13, 1958. The Congresses will have the following sections:—

Tropical Medicine

Helminthic Infections
Protozoal Infections
Bacterial and Mycotic Infections
Virus and Rickettsial Infections
Tropical Physiology
Tropical Hygiene and Sanitation.
General.

Malaria

Parasitology
Clinical
Epidemiology and Control
Malaria Eradication

All enquiries should be addressed to the Secretary General, Professor Manuel R. Pinto, at the Instituto de Medicina Tropical, Lisbon, Portugal.